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## Original Articles and Clinical Cases.

## THE CHROME-SILVER METHOD. A STUDY OF THE CONDITIONS UNDER WHICH THE REACTION OCCURS AND A CRITICISM OF ITS RESULTS.

*(Being the Presidential Address to the Neurological Society for 1896.)*


BY ALEX. HILL, M.D.

*Master of Downing College, Cambridge.*


THE silver-method, discovered by Professor Golgi, of Pavia, has thrown more light upon the structure of the central nervous system than all other methods, microchemical, physical, and experimental, put together. In the address which Professor Schäfer delivered as President of this Society, in 1893, he gave a masterly account of the logical effects which these discoveries must have upon our views as to the constitution of grey matter and as to its mode of action as an apparatus for the distribution of nerve impulses.

The modifications in our hitherto accepted beliefs upon which Professor Schäfer insisted were chiefly of a negative character, but there was enough of reconstruction to show that no question is of such burning interest as this to anatomists, physiologists, and psychologists, or shall we say, in one word, to neurologists.

In 1865, Deiters pointed out the fundamental distinction between the axis-cylinder process and the protoplasmic pro-

cesses of a nerve-cell. In 1871, Gerlach gave expression to the usually accepted view as to the structure and mode of action of the nerve-machine. Gerlach's theory was extremely simple, and yet it made all the processes of nerve activity, from reflex action to thought itself, easily explicable. We could, in fancy, follow the afferent impulse as it traces its way along lines of least resistance through the network of nerve-strands to the appropriate efferent fibre: nay, we could see impulses which had sunk out of consciousness, taking a dynamic attitude within the cells in which they had lain dormant, and starting on a fresh voyage through the network, coming into relation with other impulses similarly liberated—combining, disparting, interweaving the tissue of a dream or a thought. The apparatus by which these processes are carried out was supposed to consist of afferent fibres ending in a network which receives also the protoplasmic processes of the nerve-cells, of which the axis-cylinders become nerves. Nothing could be simpler or more satisfactory. Without some such conception, the brain, as a mechanism, becomes unthinkable, for it bears no relation in character to the products of its own activity.

But this simple faith received a terrible shock when, in 1875, Golgi introduced his method for colouring the brain with silver. This method revealed the existence of branching systems hitherto unsuspected—the collateral ramifications of axis-cylinder processes and of posterior root fibres—and, at once, our views as to the way in which grey matter does its work fell into a state of chaos.

Golgi himself could not get free from the prejudices in which he had been brought up, but he deduced from his facts the only conclusions which were logical from his point of view. He had discovered a second *plexus* formed by the collaterals. He did not want two; and, moreover, he traced the protoplasmic processes of the cells into connection with blood-vessels and ependymal cells. Hence he was justified in throwing Gerlach's plexus overboard, and accepting, as a reflex apparatus, in its stead, the plexus of collaterals. Protoplasmic processes he relegated to an ancillary position, for he regarded them as nutritional; the roots

by which cells suck up the nourishment they require both for themselves and for the long fibres to which they give rise.

Fancy the grand branching system of a Purkinje-cell reduced to the level of a vegetable root! The position seemed intolerable, and besides we have no analogy for supposing that any animal cell needs such a system of roots, however extensive may be the processes of the cell body which look to it for their nourishment, or however important their functions. Indeed, it might be pointed out that the nerve-cells which are responsible for the nutrition of the longest fibres of all, the cells of the root-ganglia, are described by Golgi himself as destitute of this apparatus for collecting nutriment. Again looking at the question from another point of view, the processes of the granule cells of the cerebellum seem to lose their meaning if the protoplasmic processes of the Purkinje-cells are incapable of collecting impulses; so, too, in the olfactory bulb the glomerular protoplasmic processes of the mitral cells seemed clearly to be the chief centripetal conductors, and not to play a subsidiary part as Golgi suggested. Then the axis-cylinder processes of the large cells of the anterior horn of the spinal cord do not carry collaterals; in this case, therefore, impulses carried to the cord by posterior roots or by descending pyramidal fibres can only be transferred to the efferent root fibres *viâ* the protoplasmic processes of their cells of origin.[1] These and a variety of other reasons justified histologists in rejecting the nourishment-collecting theory of the function of protoplasmic processes.

The changes in our views as to the mode of working of grey matter are sufficiently startling, however, even though we do not classify cell processes as functional and vegetative. With regard to many of the features revealed by the chrome-silver method we have no physiological theories at all, and some seem to be incapable of explanation. From

[1] Kölliker ("Zur feineren Anatomie des centralen Nervensystems," II., *Zeitsch f. w. Zool.*, li., p. 27, 1891) says that he cannot find collaterals on the axis-cylinder processes of motor cells. I also have searched for them in vain. Golgi figures them. Ramón y Cajal says that he observed them both in the rat and in the dove. We may therefore conclude that they are present exceptionally.

every point of view, therefore, it is essential that we should come to understand the conditions under which this method works, and learn how far we are to trust its results.

The suspicion with which we approach it would be unwarrantable in the case of almost any other method; but in many ways this method seems to court suspicion. To begin with, it is so coarse, from the point of view of modern histological technique, that we can say without any want of gratitude to the histologist who gave us this marvellous process, that it can have been discovered only by accident. A block of tissue soaked in bichromate of potassium, or in a mixture of bichromate of potassium and osmic acid, is dropped into a solution of silver-nitrate. A copious precipitate of bichromate of silver of course occurs. We should have expected that this precipitate would be uniformly distributed throughout the mass, whereas we find that the bichromate of potassium leaves the mass more quickly than the nitrate of silver enters it, and that after all the chrome-salt, which is in solution at the time, is precipitated, the nitrate of silver continues to penetrate and is reduced by certain cells and fibres in the interior of the block. The addition of a very little formic acid (about 1 to 300 of the bichromate and osmic acid mixture) delays the precipitation of chromate of silver, inducing it to crystallise out instead, and so favours the entrance of the silver-nitrate; as a result the interior of the block is freer from granular deposit than when nitrate of silver alone is used.

The cells and fibres which reduce the silver-salt are marked out with marvellous delicacy and present figures of great beauty, but the success of the method depends upon its failure—its failure as a stain. If the colour were to be taken by all the elements, or even by all the elements of one kind, the result would be an impenetrable black mass. It is because it picks out one cell in fifty, or one in a hundred that a picture is obtained which conveys information as to the structure of the tissue.

The results obtained by this method are so conspicuous and diagrammatic that no special skill in microscopy is needed for their recognition. So diagrammatic are the figures that

those who first used the method thought it quite unnecessary to copy them. More effective pictures could be made by merely imitating their general style. For a long time histologists were in doubt as to how far the artist followed nature, and how far he might be said to keep step with, or even to precede, her. These jet-black figures, on a tawny ground, are particularly suitable for photography; and this, as it seems to me, is by far the best way of reproducing them. They should only be drawn by hand when, as is not infrequently the case, the sections are too thick to allow of their photographic reproduction.

I have no intention of recapitulating the results obtained by Golgi and his pupils, by Ramón y Cajal, Lenhossék, Kölliker, Retzius, Van Gehuchten and others who have used the method with conspicuous success. Exhaustive, analytical, and bibliographical notices are accessible to everyone.[1] My endeavour has been to ascertain the CONDITIONS UNDER WHICH THE METHOD WORKS; THE NATURE OF THE REACTION; and, incidentally, THE VALUE OF ITS RESULTS. It has made startling revelations. How far may they be trusted?

What is the nature of the reaction? Why does it select certain cells or fibres and neglect the rest? Are there any cases in which the results obtained by Golgi's method are incompatible with those obtained in other ways, and if the two results cannot be reconciled, which is to go to the wall? These are the problems which I set myself to work out, and I may as well say at once that I am as far from knowing the answers as when I started. I can only hope that the publication of my work may save some other investigators trouble.

[1] *Cf.* v. Lenhossék, "Der feinere Bau des Nervensystems im Lichte neuester Forschungen," Berlin, 1893. Kölliker, *loc. cit.*; also "Handbuch der Gewebelehre des Menschen," vol. ii.; "Elemente des Nervensystems," 1893. Retzius, "Biologische Untersuchungen," *Neue Folge*, iii., iv., v., vi. Cajal, "Les nouvelles idées sur la Structure du Système Nerveux," trans. by Azoulay, 2nd edition, Paris, 1895. Van Gehuchten, "Le Système Nerveux de l'homme." Lierre, 1893. Aldren Turner, "On recent applications of Golgi's Method to the Study of the Nervous System," BRAIN, 1893, vol. xvi., p. 259. Schäfer, Quain's "Anatomy," vol. iii., part 1, 1893. Obersteiner, "Anleitung beim Studium des Baues der Nervösen Centralorgane," 3rd edition, Leipsic, 1896.

*Method.*—The conditions necessary for success, as laid down by those who have chiefly used the method, may be summed up as follows :—

(1) The subject should be a young animal or an embryo.

(2) The tissue must be as fresh as possible.

(3) It must be cut into thin blocks, not more than 2 mm. thick.

(4) During hardening, the bottles must be kept in the dark[1] and warm.

(5) If embedded in celloidin, the embedding process must not occupy more than an hour (for fear of destruction of the stain by absolute alcohol), and the celloidin should be set with 70 per cent. alcohol, and cut under alcohol.

Probably all these precautions are desirable under certain conditions, but that none of them are essential is shown by the photograph (fig. 1) from one of the most successful preparations I have ever made. It was taken from the brain of a man who had been dead for more than twelve hours; it was hardened in the cold of winter, kept in the light, embedded in celloidin in the ordinary way (the process extending over two or three days), and cut frozen on a Swift's microtone.

We are still so far from understanding the nature of the reaction, that all variations of procedure are possible sources of instruction. My object being not to get good specimens, but to determine the conditions under which the reaction occurs, I endeavoured to ascertain the limits within which the process may be varied without abolishing the reaction, and have noted the effects of the several modifications.

First, as to *material*.

(*a*) *Age of Subject.*—For general purposes young animals are desirable. The method succeeds well with embryos after about half-time (in the case of the calf, horse, and other large animals); new-born animals give excellent preparations of cortex cerebri, spinal cord, &c.; nevertheless, the most comprehensive results are obtained with animals of some days old, *e.g.*, kittens of three to twenty days, puppies

[1] In his later publications, Ramón y Cajal says that it does not matter whether the preparations are kept in the dark or in the light.

of a fortnight, rats of eight to twelve days, hedgehogs of nine days, &c.

For the cells of the cerebellum and cortex cerebri, I prefer a full-grown animal.

For the collaterals of posterior root fibres, it seems to be necessary to use a young animal: but this rule does not hold good for the axis-cylinder collaterals of pyramids and Purkinje cells. I have obtained beautiful preparations of axis-cylinder collaterals from the brains of full-grown hedgehogs.

Ramón y Cajal and Van Gehuchten recommend the use of embryos or very young animals on the ground that it is the non-medullated, or not yet medullated, fibres that give the reaction: but neither of the histologists just quoted states explicitly, so far as I am aware, that medullated fibres will not take the stain. This is a matter to which I have given some attention, in the hope that it might throw light upon the nature of the reaction, and I have come to the conclusion that although embryonic fibres and non-medullated fibres give it best, it is also possible to obtain the reaction through the medullary sheath. When Weigert and Golgi preparations are compared, it is found that the stainings do not tally. In the cortex cerebri or cerebelli, for instance, the Weigert stain follows the fibre close up to its cell: while in the Golgi preparations, the axis-cylinder process is stained black for a long distance. Again, in the white matter of the brain, *e.g.*, the internal capsule, it often happens that the silver colours great masses of fibres where we have no reasons for supposing that non-medullated fibres preponderate.

(*b*) *Freshness.*—It is especially desirable for this method of preparation that the tissue should be fresh, since the mixture of osmic acid and bichromate of potassium penetrates very slowly. If a block of two millimetres in thickness is taken out of the hardening agent after twenty-four hours and cut across, the centre will usually be found to be perfectly uncoloured, and it is easily to be understood that many *post-mortem* changes may have occurred in the interval, especially if the bottle has been kept warm.

I prefer to open the chest of the animal before the heart has ceased to beat, and then, having thoroughly washed out the blood-vessels with salt solution under suitable pressure through a canula inserted in the aorta, to inject a considerable quantity of bichromate of potassium into the circulation.

In my first attempts to inject warm bichromate of potassium into the living vessels, I found that the small arteries closed so vigorously against the irritant fluid that it was impossible to drive it through. By the addition of 1 per cent. of ordinary fermentation (ethilidine) lactic acid to the salt-solution I succeeded in producing such a paralytic dilatation of the small vessels, as judged by the free outflow from the cut jugular vein, that when the bichromate solution was used it flowed through with the greatest facility. Tooth has found that the injection of morphia after the salt-solution is equally effective in producing paralysis of the arterioles.[1] Sometimes I use the bichromate and osmic mixture for the injection, but it does not appear to possess any advantage over the bichromate alone; while in the quantity I use (250 cc. of the mixed osmic and bichromate) the cost is considerable and the smell extremely disagreeable.

This question of the *penetration of the hardening fluid* is, I believe, a factor of great importance in determining the subsequent reaction.

The excellent results which are to be obtained with the hedgehog's brain seem to be due, at any rate in part, to its unusual firmness and permeability; the difficulty in staining the human brain, to the closeness of its texture.

The success of the method when applied to young animals appears to me to depend partly upon the ease with which the hardening fluid, and, subsequently, the silver-nitrate penetrate.

Of much more consequence, as guiding us in forming an estimate as to the amount of reliance which we are to place upon the appearances presented by Golgi-preparations, is the fact that, in any part of the brain, the staining is more abundant and conspicuous when the tissue presents an open tex-

[1] Tooth, BRAIN, vol. xv., 1892, p. 400.

FIG. 1.

A cell of Purkinje from the cerebellum of a man aged 45, together with the branching system of a second cell.

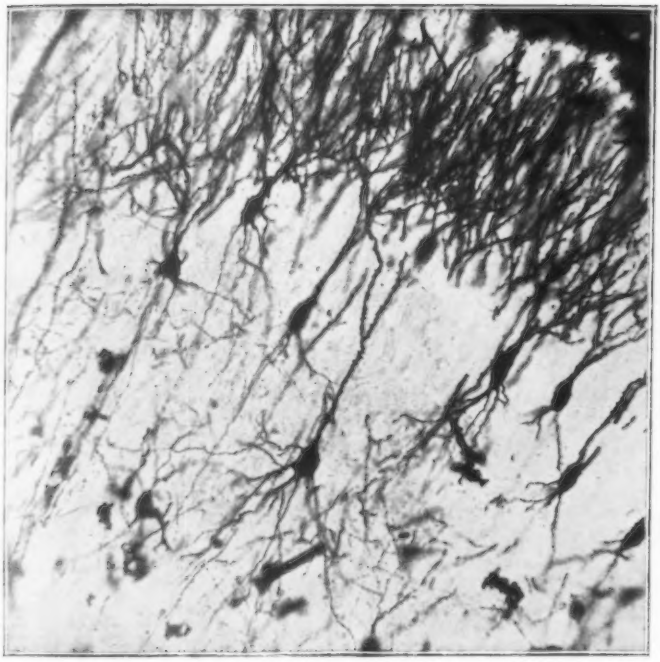

FIG. 2.

Adult hedgehog; cortex cerebri × 400. The tissue was embedded in celloidin, thickened very gradually, the process extending over four days. A thin, flat section could be obtained in consequence. The thorns on the protoplasmic processes are well seen.

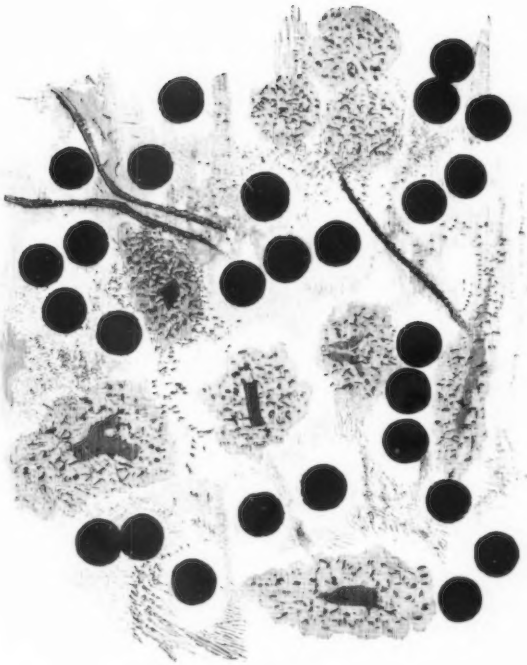

FIG. 3.

Skate (*Raia batis*); granular layer of the cerebellum, stained with the alum-carmine-Weigert method. The figure shows the nuclei of "granules" surrounding clumps of molecular substance. In the centre of the molecular clumps are seen the swollen axis-cylinders of the rosettes of Cajal's mossy fibres.

FIG. 4.

Adult hedgehog; cerebellum × 408. A single large cell of the molecular layer, with thorny protoplasmic processes and an axis-cylinder process from which a branch passes inwards to form a basket (only partially coloured) around a cell of Purkinje.

ture than it is where the tissue is dense. Many illustrations of this law may be cited; I will content myself with two which appear to me to be of the greatest importance: (*a*) In the cerebellum the thin sheet of tissue in which the bodies of the Purkinje-cells lie is extremely open, especially after the shrinking of the cells in the hardening agent. As a result we obtain in this layer an abundant staining of the fibrils which pass through it. Various appearances, often completely limited to this thin stratum, are seen in consequence. Sometimes the sheet is pierced by multitudes of vertical fibrils, the centrifugal fibrils of the "granules." At other times, either the branching processes of the tangential cells of the molecular layer or the branching processes of penetrating nerve-fibres are abundantly stained as they lie in this sheet.

The fascia dentata affords another illustration of the limitation of the stain to a layer. It usually happens, in a transverse section of the cerebrum, that we find that the cells of the granular layer of the fascia dentata, where it lies near the surface, are beautifully stained; the underlying cells of the nucleus fasciæ dentatæ may or may not be stained; the small pyramids of the granular layer where it lies at a distance from the surface are hardly ever stained, but we see in their place a quantity of penetrating fibres (fig. 7). The difference in staining of the fascia dentata in its two parts can only depend upon the relative freedom of access afforded to the reagents. Usually the fibres in the deep-lying fascia dentata are absolutely limited to this layer which is marked out by the total absence of stain on either side of it. It seems to me difficult to account for this limitation of the reaction on any hypothesis other than the one I have put forward, viz., that the reaction occurs most readily where the tissue is loosest in texture.

(2) The occurrence of the reaction does not appear to depend upon the tissue being fresh, for it can certainly be obtained a considerable time after death—at least two days in cool weather. If it were not for the slowness with which the hardening fluid penetrates, good results might, I believe, be relied upon with any tissue in which putrefaction had not already set up.

On the other hand, my experiments in injecting tissues with bichromate during life seem to show that absolute freshness has a good deal to do with the character of the results obtained. When the injection has been successful—and it is easy to tell from the appearance of the unstained nuclei whether this is the case—not only are deeply lying structures, such as the corpus striatum, stained before the pyramids, but all the cells show the most remarkable clearness of outline. The processes of the cells are sharp and clear cut, and there is in such preparations as I have made a total absence of "thorns" or "mossiness." To this I shall refer later on.

(3) *Size of the Block.*—As observed by everyone, the amount of osmic and bichromate mixture used to harden the brain should be large relatively to the amount of tissue, but the brains of different animals vary immensely in their capacity for absorbing the reagent. Of all the animals I have used none allows the reagent to penetrate so easily as the hedgehog. A complete transverse section of the brain of the young hedgehog is easily stained throughout its whole extent, giving a perfect result, even though the slab of tissue be 3 or 4 mm. thick. I attribute this penetrability to the peculiar texture of the brain which, when fresh, is white, and so firm as to be convenient to handle.

If the blood-vessels are injected with warm bichromate of potassium, the amount of tissue hardened in one block may be almost indefinitely increased, since the nitrate of silver finds its way through any thickness of tissue, giving apparently a better result the farther it has to go.

(4) *Duration of Hardening.*—In one paper (*Rivista trimestrial de histologia*, March, 1889, p. 104) Ramón y Cajal gives the following general rule:—

For neurogleia, harden 12-20 hours.
,, nerve-cells ,, 20-24 ,,
,, nerve-fibres ,, 24-36 ,,

In another place (*La Cellule*, vii., 1891, p. 130) he amplifies his directions by pointing out that the time needed depends not only upon the structure which it is

desired to show, but also upon the kind of animal and its age. For example: "In the embryos of mice, rats and rabbits the cells impregnate in a very uncertain fashion; on the other hand, the epithelial elements, vessels and fibres colour constantly, provided the duration of the hardening is not prolonged beyond two to three days. The duration of the hardening of the blocks in the osmio-bichromate mixture ought to be prolonged to two, three to five days when dealing with new-born mammals of a certain size (rabbit, guinea-pig, cat), et, à plus forte raison, s'ils sont âgés de 8 à 15 jours."

"To succeed in colouring the cells of the molecular layer in the rabbit (eight days old) the hardening must be prolonged for nearly five days; while the collaterals of the white substance demand six or seven."

Lenhossék ("Der feinere Bau des Nervensystems," Berlin, 1893, p. 6) gives as the most favourable time for the human spinal cord—

Neurogleia, 2-3 days.
Nerve-cells, 3-5 days.
Nerve-fibres (collaterals), 5-7 days.

When I commenced this series of tests it was my intention to compare Golgi-preparations of all parts of the brain with sections stained according to my modification of Weigert's hæmatoxylin method.[1] I wished to ascertain whether the silver colours tissue only, or whether, as was suggested by Rossbach and Sehrwald, in 1888, it colours instead of, or in addition to, the neurogleia and nerve-tissue, lymph, or lymph-deposit, or lymph-coagulum which surrounds the nervous structures. I was soon convinced that

[1] My modification of Weigert's method depends upon a previous staining of the tissue *en bloc* in carmine-alum. The carmine-alum is made by boiling *an excess* of both carmine and alum in a porcelain dish for three or four hours, water being added from time to time. The fluid is allowed to stand for some hours, and then filtered. Blocks of tissue are soaked in carmine for twenty-four hours; sections are then made and stained according to Weigert's hæmatoxylin method; decolouration may be effected with either ferridcyanide of potassium or permanganate of potash, the solution being in either case of about half the strength usually recommended. All nerve-cells and their processes are stained black; medullated fibres are stained blue, and non-medullated fibres black (*cf.* the photograph, fig. 13).

while the black reduction-substance may lie entirely outside the nerve-elements, forming a case for them, or may both surround and penetrate the nerve-elements, it is, in the most successful preparations, limited to the nerve-elements themselves. I therefore abandoned the comparison with Weigert preparations. For the sake of the comparison, however, all my earlier preparations were made under rigidly uniform conditions, the tissue remaining in the hardening fluid for exactly five days. Among these preparations I find admirable examples of cells of all kinds, of granules, fibres, collaterals, &c.; and hence this test, as well as my recent experiments in which I have varied the time of hardening within the widest limits (one day to two months), fail to establish anything like a definite relation between length of hardening and elements stained. Preparations of the cortex of a twelve-day rat, which had remained in the bichromate and osmic mixture for two months, exhibit pyramidal cells with their axis-cylinders and collaterals with exceeding beauty and completeness.

Ramón y Cajal says that some elements may be lost because the hardening in bichromate of potassium has been too prolonged. Of this I have never seen proof.

That pieces of tissue which after three, four, or five days' hardening give very little reaction may give a good result at the end of ten days or a fortnight I am fully convinced, but I cannot lay down any law as to the form which the improvement will take.

The variability of the result leads us to hope that when we understand the conditions under which the reaction occurs we shall have in our hands a method with which to produce at pleasure a wide range of effects, and it is very greatly to be hoped that someone will undertake an exact series of observations upon its time- and temperature-relations.

Prolonged immersion in silver-nitrate does not appear to affect the reaction.

(5) *Temperature.*—I have hardened the tissues at every temperature from the cold of winter to 45° C. Warmth hastens the reaction, but it does not, so far as I can determine, affect its quality.

(6) *Light.*—As observed elsewhere the reaction occurs in bright sunlight as well as in photographic darkness.

(7) *Celloidin.*—The rules for embedding, as laid down by various observers,[1] present considerable discrepancy although all agree that the sojourn in the alcoholic solution of celloidin should be as short as possible. I have prolonged it up to four days without any perceptible deterioration, and with the obvious advantage that the celloidin when set and cut does not pucker but lies perfectly flat on the slide. The accompanying photograph (fig. 2) is from a section of a block placed for some hours in a mixture of alcohol and ether, to which celloidin was added in gradually increasing quantities until at the end of four days it was ready to set. It is a matter of great importance, if celloidin is to be cut frozen, that its constitution should be uniform. I am in the habit of gradually adding dry celloidin to the alcohol and ether in which the block is soaked. Not only does this ensure penetration, but the sections when cut lie perfectly flat. It is just as easy to make a section of the whole brain, either transverse or longitudinal, as to cut a minute piece.

*Variations in the Hardening Agent.*—There is little latitude for variation in this direction. A chromate of some kind must be used, and the potassic bichromate seems to answer better than other salts. Ammonic bichromate gives the reaction, but whilst the cells come out very clearly, and the fibres are clearer than with potassic bichromate, the finer structures are not seen.

Salts of chromium, other than the chromates, do not give the reaction. Chrome-alum, for example, which for some purposes is an excellent hardening agent, is, for this method, perfectly useless.

Osmic acid expedites the hardening, but does not take part in the reaction; indeed, it may be replaced by formaline

[1] Ramón y Cajal: "The pieces can be quickly embedded in celloidin or paraffin." Kölliker: "One hour in absolute alcohol and one hour in celloidin." V. Gehuchten: "Fifteen to twenty minutes in 96 per cent. alcohol, a quarter of an hour in absolute alcohol, a quarter of an hour in thin celloidin. The block is fixed on cork with celloidin, and immersed for a short time in 70 per cent. alcohol." Lenhossék recommends five minutes in a moderately thick celloidin solution; placing the object in elder-pith; setting celloidin with 80 per cent. alcohol, and cutting under alcohol.

(4-6 per cent.), as Durig[1] has shown. There is, therefore, no need for such a cumbrous name as bichrom-osmio-silver method (Retzius): the "chrome-silver method" best expresses the reaction.

*Variations in the Silver-salt.*—The only experiments I have tried have been in the direction of a salt more easily reducible than the nitrate.

(*a*) Silver-acetate gives the reaction, but does not pick out the finest markings, and is usually accompanied by a great quantity of deposit.

(*b*) Silver-nitrite, saturated solution, *i.e.*, about $\frac{3}{4}$ per cent. (with the addition of formic acid about 1 to 1,000 parts of the nitrite solution), gives an excellent result. The reaction seems to differ from the reaction obtained with the nitrate in certain important respects, and I am hoping that this will prove a useful modification of the process. So far as my observations go at present, they lead me to think that the nitrite gives a better reaction with the extremely minute fibrils than the nitrate; it gives a good preparation of collaterals; it shows granules lying in an abundant feltwork of fibrils; the branches of protoplasmic processes are more numerous, and their "thorns" more distinct than when nitrate is used.

*The Nature of the Reaction.*—The term "stain" has been generally abandoned since it is clear that the reaction which occurs when a tissue soaked in bichromate of potassium is plunged into a solution of nitrate of silver is not comparable to a process of staining by an organic stain. Ramón y Cajal speaks of the black colouration as a "deposit of chromate of silver."[2] Van Gehuchten refers to it as a "reduction." In fortunate sections the chief colouration is black, without a tint of either green or red. There is almost always in the same sections a red-brown colouration of blood-vessels and other structures similar to the effect produced upon fresh tissue (especially intercellular "cementing substance") by the action of silver-nitrate alone. The extreme blackness

[1] Durig "Das Formalin als Fixirungs mittel anstatt der Osmiumsäure bei der Methode Ramón y Cajal's," *Anat. Anz.*, x., No. 20.

[2] Ramón y Cajal, *La Cellule*, vii., p. 131 and elsewhere.

of the black deposit makes it quite clear that it is not a chromate of silver. It must be a reduced salt (sub-salt) of silver. That it is not a metallic oxide or a salt reduced so far as in photography is shown by the solubility of the deposit in hyposulphite of soda or dilute ammonia.

One of the most singular peculiarities of the deposit is its rapid disappearance when the section is covered with a coverslip. All the "staining" may disappear, if the section is mounted in ordinary Canada balsam, in four or five hours, although masses of black deposit remain permanently. Since most of the gum-resins have a weak oxidising action, the disappearance of the colour might be attributed to the oxidation of the reduced silver-salt. If, however, the process is watched under the microscope, appearances are noticed which indicate that the change is due, as Sanassa suggested, to physical causes—at any rate, in part. The colour first leaves the centre of cells or fibres. Dark brown granules then appear in the matrix in the vicinity of the structure which is losing its stain, and it would seem as if the deposit is withdrawn from the tissue by a mechanical force; perhaps its displacement is due to currents set up by the drying of the balsam at the edge of the coverslip. I find that when a slowly-setting turpentine balsam is used without a coverslip, the colour stays in the section, even though the balsam about it may remain liquid for days. On the other hand a large part of the stain is permanently retained in a covered section if the balsam has been evaporated until it sets in a brittle mass, and then re-dissolved in xylol or chloroform. Preparations made with nitrite are also comparatively durable, and the fact that hyposulphite of soda does not destroy all the colouration shows that the reduction is more complete in some parts (particularly the cells and their protoplasmic processes) than in others, and holds out a prospect that a modification will soon be discovered which will ensure the permanence of the preparations when covered with a cover glass. Various methods have been suggested for fixing the silver-deposit —methods which naturally occur to every photographer. It may be toned in an alcoholic solution of chloride of gold

(Obregia[1]), or converted into a bromide which is subsequently reduced by light (Greppin[2]), or the reduction may be completed by sodic sulphide, eikonogen, or any other developer, and it may be mounted beneath a coverslip with or without subsequent toning with gold or with platinum. It is very easy in most cases to obtain a preparation which is permanent, although covered, but there is always, so far as my experience goes, a loss of delicacy. If reduction is completed by a developer, the ground-substance, which still retains traces of silver-nitrate, either free or in chemical union with proteids, is darkened. If development is not completed before toning, some of the finer markings are lost.

I find that good covered preparations may be obtained by staining in fuchsin, with subsequent treatment with picric acid in spirit, and washing. Such preparations are usually too dark, but may be of use in showing the position of the black structures in relation to other cells and fibres.

What is the nature of the chemical substance which, when united with a chrome-salt, reduces the silver? It might be *doubted whether a chrome-salt is necessary*, but such experiments as I have tried seem to show that it is. All my attempts to reverse the process, using the silver first and the bichromate of potassium afterwards, have failed, even when nitrate of silver or lactate of mercury was passed through the cerebral blood vessels. Again, if acetate of copper is used after the chromate it prevents the reaction unless the block is returned to the chromate for a time, in which case it takes the stain as usual.

The fact that the preparation for the silver-stain is effected by a chrome-salt suggests that the reduction or non-reduction of the silver-salt depends upon the extent to which the chromate is fixed by light. Chrome-salts, as is well known, are profoundly changed by the action of light. If a gelatine plate be immersed in a chromate and then exposed

[1] Obregia, "Fixirungsmethode der Golgischen Präperate," *Virchow's Arch.*, cxxii., 1890, p. 387.

[2] Greppin, "Weiterer Beitrag zur Kenntniss der Golgischen Untersuchungsmethode der Centralen Nervensystems," *Arch. f. Anat. und Physiol.*, Suppl. Heft., 1889, p. 55.

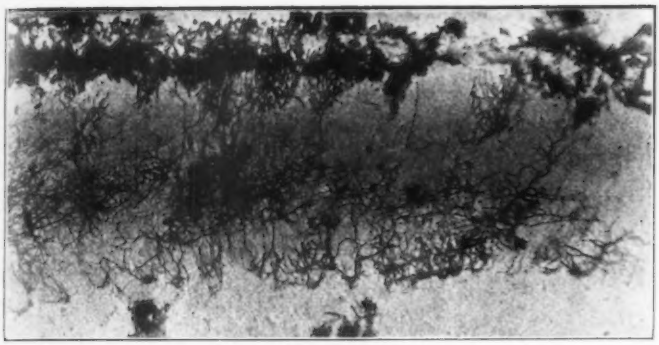

FIG. 5.

Adult cat; cerebellum. Large cells of the molecular layer are seen forming baskets about the cells of Purkinje. The cells of Purkinje are not coloured, but portions of their branching systems are shown at the top of the molecular layer.

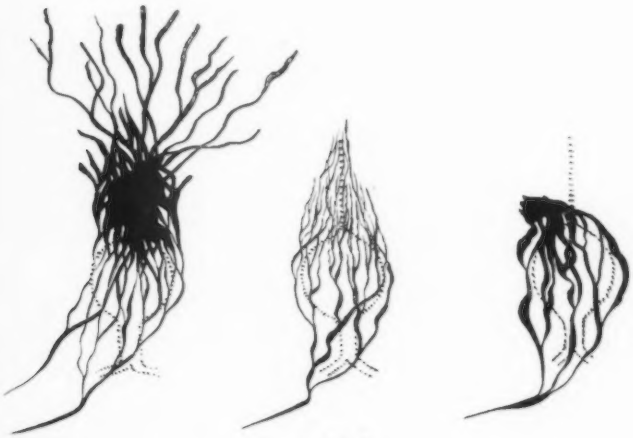

FIG. 6.

Diagrams of the three types of "basket" found in the cerebellum:—

(*a*) The appearance most commonly observed.
(*b*) The tassel of separate fibres figured by Cajal.
(*c*) The tassel ending in a black mass beneath the cell of Purkinje and fibres streaming off from this mass into the granular layer.

FIG. 7.

Adult hedgehog; fascia dentata hippocampi. Showing on the superficial side of the fascia dentata the colouration of cells, while only fibres are stained in the part farthest removed from the surface. This indicates the effect which the texture of tissue has upon the chrome-silver reaction.

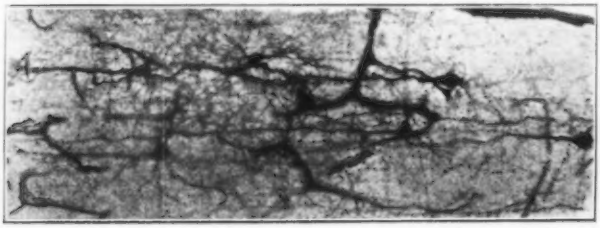

FIG. 8.

Rat, 4 days old; cortex cerebri. The apical process of one pyramid runs into the base of another more superficially placed.

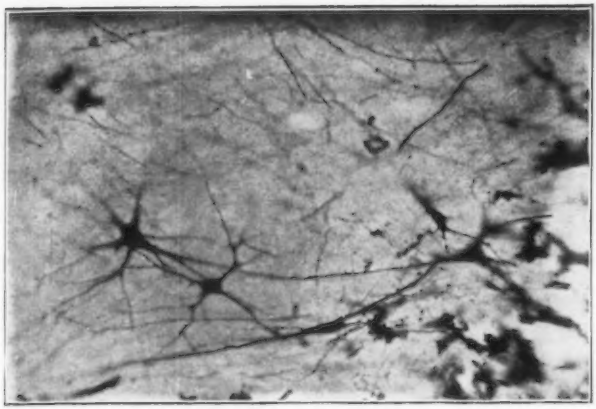

FIG. 9.

Calf, six months (*Octus*), spinal cord. Showing the connection of anterior horn cells by stout processes.

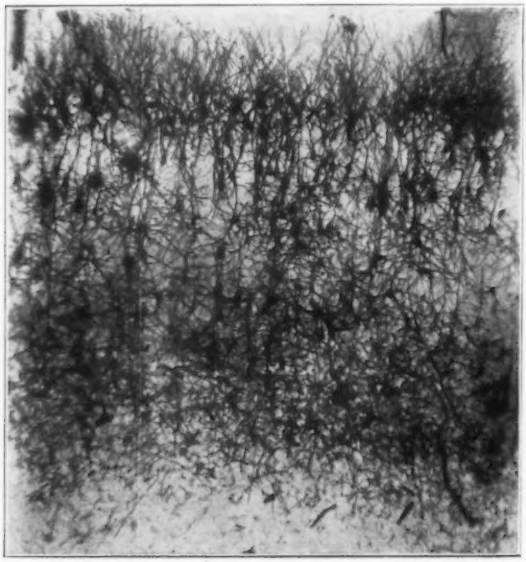

FIG. 10.

Adult hedgehog; cortex cerebri. The vessels were injected with warm bichromate and osmic mixture. The protoplasmic processes of the pyramids are destitute of thorns.

FIG. 11.

Adult hedgehog; cortex cerebri. Showing the junction of Meynert's second and third layers. The protoplasmic processes of the pyramids are thorny.

to the light (as in one of the methods used in preparing plates for photo-printing), the chrome-gelatine compound upon which the light falls is rendered insoluble. It seemed possible that light penetrates the blocks of brain immersed in bichromate of potassium and reaches some cells while it is blocked out from others, but various experiments which I have made show that this is not the explanation. For instance, I divided a brain into two halves; put one half, in suitable pieces, into a bottle of bichromate and osmic which was enveloped in black paper and kept in the dark throughout all stages of the preparation, only bringing the pieces into the light when they were placed on the microtome. The other half of the brain was exposed throughout all stages of its preparation to the full light of a west window. The reaction succeeded equally well in the two cases, although the results were somewhat different. It seems unnecessary to record the differences in detail, since they may be attributed either to the caprice of the method, or to the fact that the bottle exposed to the light was warmed by the afternoon sun while the other bottle was kept at a uniform temperature.

The fact that in one part of a section the stain will mark out the nerve-cells and in another the neurogleia, precludes us from looking to any chemical body peculiar to nervous tissues as the attractive substance. The singular way in which in all sections one element, whether large nerve-cell, small nerve-cell, or nerve-fibre is picked out, while a dozen, a score, or perhaps hundreds of precisely similar elements are passed by, suggests that the condition of nutrition of the cell determines its reacting power.

*Does the reaction depend upon the condition of nutrition of the elements?*—To test this by exhausting one part with repeated stimulation while another part remained at rest was a natural suggestion; but the fact that the method so often selects the neurogleia cells led me to doubt whether any result would be obtained. It seemed better to try to affect the nutrition of the whole of the brain at once and profoundly. With this end in view, I determined to wash the blood out of the brain, and to compare this starved

brain with one removed from an animal before the cessation of the circulation.

(1) A stream of salt solution (·6 per cent.) at the temperature of the body, was passed into the aorta of a puppy for more than half-an-hour. The water left the jugular vein quite free from colour; but the brain took the silver reaction in the usual way.

(2) In the case of a second puppy, 1 per cent. of ordinary fermentation (ethilidene) lactic acid was added to the salt-solution. It was passed for more than half-an-hour, and appeared from the swelling of the body and the rapidity with which it left the pressure bottle to cause great dilatation of the blood-vessels. The brain took the reaction as usual.

These experiments, 1 and 2, were repeated in the hedgehog, and other animals.

(3) After using (in the case of an adult hedgehog) normal salt-solution for a short time, the pressure bottle was filled with a 10 per cent. solution of NaCl. It flowed freely through the vessels for more than half-an-hour. The body of the animal became greatly distended. All the connective tissues were found to be filled with transparent colourless jelly, resembling vitreous humour. The brain was semi-transparent, soft, and very difficult to handle, remarkably different from the ordinary hedgehog-brain, which is particularly firm and white. Nevertheless it took the reaction as usual so far as the selection and rejection of elements is concerned, although the appearance of the elements was changed in certain details.

The results of this last experiment seem to me very remarkable. The strong salt-solution must have dissolved and carried away a great quantity of albumins and globulins. All "cement-substance" or other lymph-deposit must have been dissolved. The softness of the brain showed that it had lost much of its substance, and yet it reacted to the bichromate and silver in the usual way. It seems quite to exclude any state of nutrition as a factor in determining reduction; at the same time it makes it very difficult for us, unless by a process of elimination, to put our finger upon the chemical substance which, when combined with a chrome-salt, reduces the nitrate of silver.

In face of this result, I did not think it worth while to carry out the experiments upon the effects of $CO_2$, morphia, chloroform, &c., which I had in contemplation.

## Interpretation of Results.

In summing up the contributions to our knowledge made by Golgi, Ramón y Cajal says[1] that the researches of this *savant* have placed *hors de discussion* the following facts:—

(1) The free termination of the protoplasmic expansions of nerve-cells, as well as of the processes of neurogleial, or spider cells.

(2) The existence in the axis-cylinder of ramified collaterals.

(3) The existence of two kinds of cellular elements, distinguished by the behaviour of their axis-cylinders; the cells in which this process loses its individuality by ramifying without reaching the white matter, and the cells of which the nervous process, despite its numerous collaterals, preserves its individuality, and continues into a tube of the white substance.

I should add to this catalogue of the great changes which the silver method has introduced into current nerve-histology:

(4) The existence in various parts of the central and peripheral nervous systems of a form of nerve-ending, first described by Ramón y Cajal the pericellular basket work; with the physiological inference that nerve impulses act upon (or from) nerve *cell-bodies*, through the medium of a brush of fibres.

(5) The conclusion that axis-cylinder processes, and their collaterals, as well as protoplasmic process have free terminations; that there is no such thing as anatomical continuity of nerve-elements, with the physiological consequence that transference of impulses occurs *in distans*.

(6) The great prominence given in making schemes of the several cortical fields other than the cerebellar cortex, to large nerve-cells, their axis-cylinder processes, and

[1] *La Cellule*, vii., 1891, p. 126.

collaterals; these elements, together with certain free-ending fibres, being held to constitute the reflex mechanism, to the exclusion of the "granules."

These changes, introduced by those who have worked with the chrome-silver method into our conception of the central nervous system, are of such importance that the grounds upon which they are based need the fullest investigation. It is our duty to assume a sceptical attitude of mind towards the new histology, in justice to the investigators who patiently laboured in this field before the introduction of the silver method. We fully realise that Golgi's predecessors did their work with tools which now seem primitive, but they worked without tiring, absorbed in their zeal for truth, and they deserve that the results of their labours should be upheld until swept from the field by an overwhelming weight of argument.

The absence of uncertainty, the simplicity, one might almost say the ingenuousness, of the silver-preparations carry all before them. It is difficult to resist the belief that they tell the truth, the whole truth, and nothing but the truth. For the purposes of this address, however, I have accepted the position of counsel for the defendants, and I beg to be allowed to lay before this court certain considerations which tend to invalidate the testimony of the plaintiff.

I will sum up the evidences of untruthfulness which tend to shake our faith in the chrome-silver method under three heads:

(1) The deposit is liable to spread beyond the limits of the elements which chiefly attract it. In some cases it stains, not the cell or the fibre, but the wall of the lymphatic space which surrounds it.

(2) The amount and character of the reaction depends upon the texture of the tissue in which it occurs. It is, therefore, liable to stop short at the edge of a favourable zone, giving an incomplete picture of the elements which it colours.

(3) *a*. It never takes all the elements of any one kind. *b*. It seldom shows heterologous elements in the same section with sufficient completeness to enable us to trace their connections. *c*. It does not stain the whole of the substance

which belongs to a cell or a fibre, but only part, and this apparently the neuroplasmic not the conducting part.

We may now consider how far these three drawbacks to the method affect the credibility of the great conclusions which have been drawn from its results.

(1) *The Spread of Deposit.*—Of this we need say but little. Everyone who has worked with the chrome-silver method is on his guard against this danger. It is especially in the case of neurogleia that the deposit is apt to occur outside the cell. I am inclined to believe, to take an example from the neurogleia, that the extraordinary irregularities on the course of the central processes of Bergmann's cells of the cerebellum, as figured by Retzius,[1] are collections of deposit. It may also occur on nerve-elements; thus it serves to exaggerate the mossiness of Cajal's mossy fibres, although the existence of these "fibras musgosas" is now placed beyond dispute. In good preparations the branching fibres of this system are of exquisite delicacy and clearness of outline. In fig. 3 the thickenings at the points of division, which constitute the "rosettes," are shown by another staining method. In passing, it may be noted that it would be a great advantage if the term *rosette fibres* could be substituted for mossy fibres, since the thickened bunches which these nerves carry are unlike any kind of moss except, perhaps, certain lichens, and, besides, the term "mossy" is constantly and aptly applied to an entirely different appearance which distinguishes the protoplasmic processes of many large cells both nervous and epithelial.

*The staining of the lymph-case* in which cells and their processes lie is a phenomenon which has not received the attention it deserves. It is of very frequent occurrence in the cerebellum. With or without simultaneous staining of the cells of Purkinje, the wall of the space in which these cells and their chief processes lie is coloured, usually a full brown, but sometimes a very dark brown or even black. It is difficult to show this in a photograph, or even in a drawing, since the appreciation of the fact that one is

[1] Retzius, "Biologische Untersuchungen," *Neue Folge*, vi., 1894.

looking at a hollow case depends entirely upon variations of focus. I am, therefore, obliged to content myself with a verbal description. Owing, no doubt, to the fact that many fibrils pass through the case, its wall is always sculptured in an elaborate but variable pattern. It frequently extends, for a short distance, outwards along the course of the fibrils which pierce it. Of course it follows the outlines of the cell and its chief protoplasmic branches.

After all that has been said about Cajal's *fibres grimpantes* (kletterplexus, climber plexus), and especially since they have been carefully investigated by Retzius, and their authenticity is vouched for by so competent an histologist, I hesitate to suggest that they are an illusion due to the silver-staining of the lining of the lymph-case which surrounds the Purkinje-cell and its processes. If I saw the preparations from which Cajal and Retzius derive their descriptions, it is probable that I should recognise at once that such an explanation is out of the question. I content myself, therefore, with asserting that the only preparations of my own which show the kletterplexus may be explained in this way.

The apparent continuity of the plexus with a nerve is a great difficulty in the way of this explanation; but, on the other hand, Cajal's description of the nerves as "fibres épaisses à myéline, peu ou pas ramifiées à leur passage à travers les grains," would apply equally well to the neural processes of the Purkinje-cells.

(3) Of much more consequence than this basket-work surrounding protoplasmic processes are the baskets supposed to be formed by axis-cylinder processes and their collaterals about the bodies of large nerve cells. They have been described in the cerebellum, the retina, sympathetic ganglia, and elsewhere. The ending of a nerve in a brush of fibrils which form a basket to invest the body of a nerve cell is a new conception in histology which we owe to the Golgi method. Have we any alternative but to accept the picture which the silver draws as a correct and complete account of the structure? I hope to show that we are *not compelled to believe that the baskets which surround Purkinje-cells are the end-brushes of nerves.*

The cells which form these baskets are found in the deeper parts of the molecular layer of the cerebellum. They were first described by Golgi as cells of his second type. No cells are easier to stain (figs. 4 and 5). In many preparations their processes form so dense a felt-work that the molecular layer is impenetrably black, although no other structures are coloured. Their full extension can only be seen in antero-posterior sections, irregularly stained.

The oval cell-body, as seen in section, gives origin to five or six processes, some of which run towards the surface, while others turn towards the granular layer. One of the processes extends horizontally for a great distance (1 to 2 mm. in the cat) giving off at intervals branches which descend towards the Purkinje cells. This long process is rightly called the axis-cylinder process of the cell; but it will be noticed (*a*) that although it is thin, round, and well-defined at its origin, it has a curious tendency to thicken as it goes on; (*b*) that it never acquires a medullary sheath (or if it has such a sheath this does not interfere with its colouration); and (*c*) it is possible that some of the other processes also take part in the formation of baskets.

As its collaterals approach the cells of Purkinje, each of them divides into a brush (the "basket"), the filaments of which end freely, and eventually the axis-cylinder process itself terminates in the same way. Ramón y Cajal, v. Gehuchten and others are perfectly explicit as to the free ending; but it is with regard to this free ending that I venture to mistrust the silver method.

If a number of specimens of baskets are examined, it will be found that much the commonest appearance is the ending of the branches which invest the cell of Purkinje in an irregular patch or blob beneath the cell (fig. 6a). This appearance is set aside as incomplete. On the other hand, instances will be found, every here and there, in which, beneath the cell of Purkinje, the basket-work, after forming a dense tuft, streams off amongst the granules as separate fibres (fig. 6c). We have, therefore, three forms of basket to select from—(1) the loose basket-work ending in a

blob beneath the Purkinje-cell; (2) the tassel of free-ending fibrils described by Ramón y Cajal (fig. 6b); and (3) the bunching together of the fibrils of the tassel and their continuation into the granular layer.

In deciding between these divers forms of basket, we need to give great weight to the influence which the open nature of the tissue forming the sheet of Purkinje-cells has upon the reduction of the silver-salt. It constantly happens that colouration is limited to this sheet—the fibres which traverse it being stained, while the molecular layer, on the one side, and the granular layer, on the other, are uncoloured. The weight which must be given to the mere physical texture of the sheet is well illustrated by the accompanying photograph (fig. 7), taken from a different part of the brain, in which the conditions are somewhat similar. Like the cerebellum on a small scale, the fascia dentata of the hippocampus consists of a layer of granules bearing a sheet of cells, each of which has an axis-cylinder process passing back through the granules and an elaborate system of branching processes which extend towards the free surface. The resemblance to the granular layer, the sheet of cells of Purkinje, and the molecular layer of the cerebellum, is very singular. This triple sheet of tissue is folded over the cortex margin or nucleus fasciæ dentatæ, and I have found in numbers of preparations of this region which I have coloured with the chrome-silver method, that whereas in the part of the fascia dentata which lies on the surface, the cells and their processes are beautifully defined, and only their axis-cylinder processes are to be seen in the granular layer, on the other side of the nucleus fasciæ dentatæ, where the tissue lies at a distance from the surface, no cells are stained, but numbers of fine fibrils are seen streaming through the granular layer. Now, it cannot be doubted that these fibrils extend beyond the limits of the granule layer, although it is only in this layer that they stain—owing, as I think, to the looseness of the tissue.

In the cerebellum, it is clear that the cells of Purkinje leave but little space for the passage through the sheet in which they lie, of the vast number of fibrils by which the

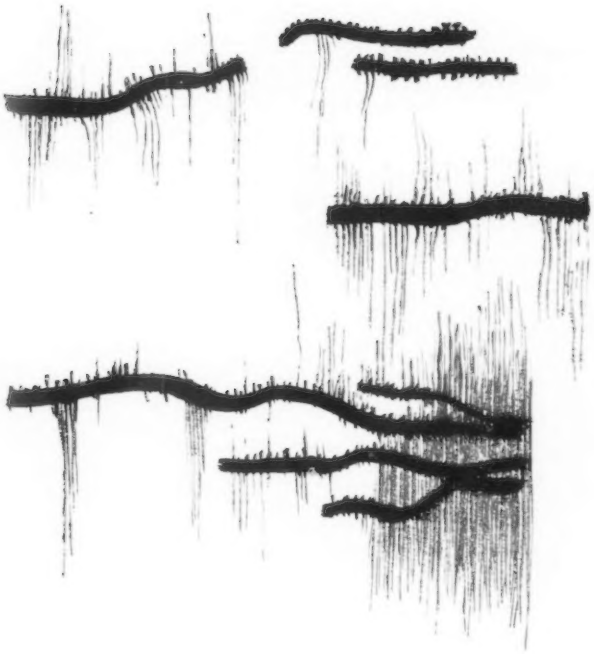

FIG. 12.

Skate (*Raia batis*); cerebellum. Sketch of the molecular layer, showing the union of horizontal fibres with the undulating protoplasmic processes of Purkinje-cells. In other parts of the preparation the processes were thorny. Here, horizontal fibrils of varying length take the place of thorns.

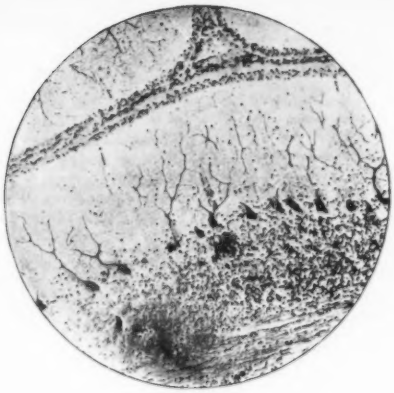

FIG. 13.

Lamb; cerebellum × 77. The section was stained with the alum-carmine-Weigert method by myself, but I am indebted to Dr. Dallinger for permission to reproduce the photograph which appears on the frontispiece of his edition of Carpenter's "Microscope."

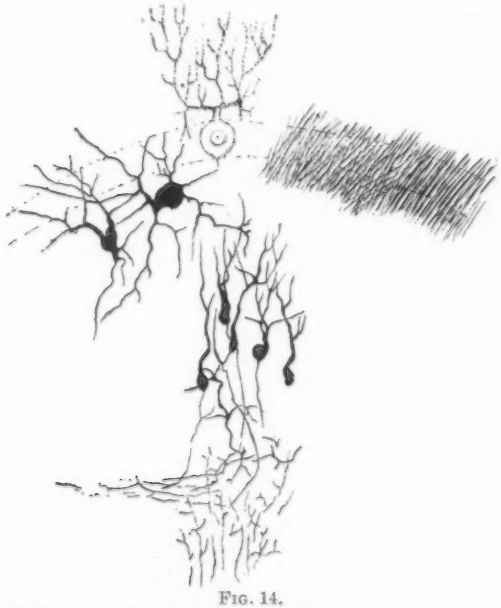

FIG. 14.

Rat, 4 days old; cerebellum. A group of granules with centripetal axis-cylinders. Two Golgi-cells are seen above the granules. The position of the cells of Purkinje is indicated by dotted lines.

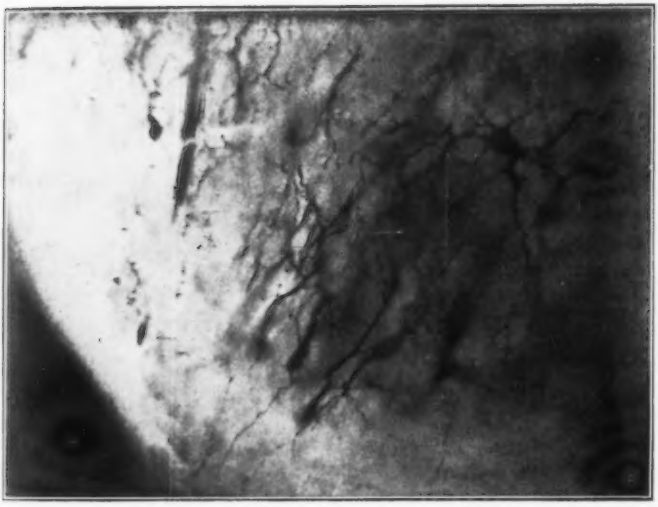

FIG. 15.

Rat, 4 days old; cerebellum × 398. Photograph of a group of granules, with centripetal axis-cylinders and a Golgi-cell.

FIG. 16.

Kitten, 3 days old; olfactory bulb × 248. Showing mitral cells and granules.

molecular and granular layers are united. These fibrils seem to me to arrange themselves in two sets: (1) the tassels of the "molecular" cells which place themselves around the cells of Purkinje, and (2) the axis-cylinder processes of the "granules" which occupy the intervening spaces. Owing to the peculiar texture of the sheet, and especially to the facilities for the passage of the silver nitrate which its radial striation affords, it comes about that the staining is much more complete here than elsewhere; BUT IT DOES NOT FOLLOW THAT BECAUSE THE FIBRILS OF THE MOLECULAR CELL TASSELS CANNOT BE FOLLOWED INTO THE GRANULAR LAYER THEY END HERE.

The object of my work is to determine the conditions and limitations of the chrome-silver method. I have no intention of giving in this paper a detailed description of any particular nervous organ; nor do I contemplate making a list of all the supposed revelations of the method which seem to me to require confirmation. These three illustrations from the cerebellum are selected merely on the ground that they are representative of the three main directions in which the *method is likely to mislead.*

(*b*) *Isolation of Nerve-Elements.*—The great conclusion deduced from observations made with the chrome-silver method is the discontinuity of the end-brushes of fibres and the ramified processes of nerve-cells. This anatomical conclusion is of profound interest to all who endeavour to explain the action of the nervous mechanism, whether physiologists or psychologists, since like the theory of which the anatomical basis has just been discussed—the theory that nerve-fibres end freely in contiguity with the bodies of nerve-cells—it is completely subversive of all existing notions of nerve-conduction.

Gerlach[1] described the posterior roots of spinal nerves as ending by ramification in the grey matter; the anterior roots as starting in cells; between the two a plexus formed by the union of the terminal twigs of the afferent fibres, the protoplasmic processes of the motor cells, and thirdly, the

[1] Stricker's "Manual of Human and Comparative Histology," translated by Henry Power, London, 1872, vol. ii., pp. 327 *et seq.*

protoplasmic processes of smaller cells which have no axis-cylinder processes. The instance—the cells of Clarke's column—from which he endeavoured to prove that certain cells have no axis-cylinder processes, was unfortunate, since it has been shown, by the same methods which Gerlach himself used, that he was mistaken. However, the existence or non-existence of cells without axis-cylinder processes is not essential, and, for purposes of comparison, it is better to suppose that they do not exist.

The Gerlachian theory, then, stands thus: the grey matter is a network; long fibres of every degree, whether destined for other parts of the homologous network or for a heterologous network (say from the grey matter of the spinal cord to the cortex cerebri) or for a motor organ, start from cells; fibres from distant cells end by ramifications; there is no functional difference between protoplasmic and axis-cylinder processes. It is very important that this last point should be understood. A good deal has been made lately of the difference in direction of conduction. Ramón y Cajal has formulated a theory, "de la polarisation dynamique des éléments nerveux;" v. Gehuchten had already given expression to the same idea in coining the two terms "cellulipetal" and "cellulifugal"; but this difference in the direction of conduction, if it be absolute, which is open to question, is a trivial and accidental distinction. The function of a nerve fibril is to conduct. We should not expect to find a difference in structure or in behaviour to reagents between fibrils which conduct towards a cell and fibres which conduct away from a cell. The two processes of a cell of a root-ganglion are of equal standing; not one "protoplasmic" and the other "neural."

The essential difference between Gerlach's teaching and the modern view (the view of Retzius, Ramón y Cajal, Kölliker, v. Gehuchten, and many others) turns upon this: —*Is the grey matter a network of continuous strands or is it a felt-work of interlacing but discontinuous fibrils?*

The importance of this distinction lies in its physiological application. If grey matter is a network, impulses are conducted through continuous circuits. If it is not a

network, their passage is an *actio in distans* (*cf.* Kölliker, *loc. cit.*, p. 35). The substitution of the term "contact" for "contiguity" does not help matters physiologically even if it were justifiable; whereas, anatomically, it is a gratuitous assumption. It is impossible for a microscopist to distinguish, in a preparation stained black, between *contact* and *continuity* of substance. Besides he has no right to conclude that the position of structures in a hardened and shrunken tissue is the position which they occupy during life. On the contrary, he knows that the tissue has lost lymph to the amount of at least one-third of its bulk.

The extreme difficulty of this conception justifies us in pushing our resistance to the verge of rebellion. I wish, therefore, to lay before you certain considerations which seem to justify us in calling for yet more evidence before we make up our minds.

(1) The belief in the discontinuity of the elements is based chiefly, although not entirely,[1] upon results obtained with the chrome-silver method. Certainly the figures which this method gives appear discrete; but what is proved by a stain which picks out one cell-system and leaves a number of similar cells uncoloured? In no preparation of the cortex cerebri, for example, could I find fewer than seven pyramids unstained for every one stained; usually the proportion of unstained cells to stained cells is much greater. Supposing for a moment that all these pyramids are united together by their protoplasmic processes, should we recognise it in a preparation in which every stained cell is surrounded by seven cells which are unstained?

Gerlach's theory, however, did not imply that *homologous elements* are united together. It is more intelligible on the supposition that the large cells (the nutrient cells of long fibres) are not directly connected with one another. Now when we endeavour to obtain evidence as to the union of heterologous elements we find that the Golgi preparations are almost silent. Hardly ever are two distinct kinds of nerve element, say branching fibres and nerve-cells, or large

[1] Forel in 1887, Retzius (using Ehrlich's method), and His (as the result of embryological research) were led to doubt the existence of the network.

nerve-cells and granules, properly and completely stained in the same part of any preparation, or even in the same preparation.

(2) Even with the chrome-silver method a coarse union between similar cells is shown to be by no means uncommon. These connections appear to be freaks in development, and are of no interest except as showing that intercellular union is possible. In fig. 8 I show a case in which the apical process of one pyramid ran into the base of another; careful focussing left no doubt as to their actual continuity. Union between two cells of Purkinje by means of a thick arched process is not uncommon. Fig. 9 shows three cells of the spinal cord connected by stout protoplasmic processes. I have seen two granules in the olfactory bulb of an adult animal united by a stout bridge.

(3) *Thorns* (épines) on the protoplasmic processes of pyramids and cells of Purkinje were first described by Ramón y Cajal, but no attempt has been made to determine their significance. I am inclined to think that these thorns will eventually give the key to the problem.

Thorns are very minute lateral branches of the protoplasmic processes of certain cells; especially pyramids (figs. 2, 11), and cells of Purkinje. They often occur at very regular intervals. Sometimes they are opposite but usually they are roughly alternate. Their length varies from less than $1\mu$ up to 5 or $6\mu$; on the peripheral processes of the granules of the olfactory bulb they often measure 10 or $12\mu$ (fig. 18). They usually terminate in minute knobs. Sometimes the knobs alone are visible. Occasionally a clear line can be recognised carrying a round dot in its centre or at one end.

Are the thorns artifacts? They certainly are most distinct in imperfectly hardened tissue. When I first succeeded in making a thoroughly successful injection of the brain with bichromate of potassium I was much struck with the fact that the processes of the pyramidal and other cells were perfectly clean cut and destitute of thorns (fig. 10), whereas tissue which had been purposely left for twenty-four hours before immersion in the osmio-bichromate mixture showed the thorns in a very marked manner (fig. 11). So, too, did

the brain injected with strong salt-solution. This led me to think that the thorns were artificial products. On the other hand, their great regularity is opposed to an artificial origin, and besides, they are not limited to preparations made with the chrome-silver method. If a section of the molecular layer of the cerebellum is deeply stained with hæmatoxyl in and then broken up with needles in glycerine, the thorns on the processes of the Purkinje-cells are beautifully distinct, although they are irregular in length and do not end in knobs.

It seemed to me that the thorns must indicate an actual union between certain unstained filaments and the protoplasmic processes. I sought, therefore, to ascertain the nature of these unknown filaments by studying the cortex of the cerebellum. As everyone knows, the molecular layer of the cerebellum exhibits a very regular striation parallel with the surface. This is seen to perfection in the cerebellum of a cartilaginous fish. In the skate, for example, the undulating processes of the cells of Purkinje, which have a radial arrangement, cross the tangential striæ at right angles, making with them a diaper pattern of the utmost regularity. Near the dorsal commissure, the cells of Purkinje are absent, and only the tangential striæ are present. In the cerebellum of the skate (fig. 12), coloured with the chrome-silver method, I am able to show in place of thorns on the Purkinje-cells, long striæ streaming away from the protoplasmic process on either side. Unfortunately, I have not succeeded in following the axis-cylinder processes of the granules of the fish's cerebellum from the granules to their divarication in the molecular layer, nor had Fusari[1] better fortune. Schaper[2] traced the fibre into the molecular layer, and observed its divarication, but could not follow it to its termination. We may therefore conclude that the arrangement of the axis-cylinder is the same as in birds and mammals, and I think that there is little doubt but that the tangential fibres which I observe in direct continuity with

[1] Fusari, "Untersuchungen über die feinere Anatomie des Gehirnes der Teleostier," *Int. Monatschr.*, 1887.

[2] Schaper, "Zur feineren Anatomie des Kleinhirms der Teleostier," *Anat. Anzeiger*, Nos. 21 and 22, 1893.

the protoplasmic processes of the Purkinje-cells, are the axis-cylinder processes of granules.

It is most probable that the tangential striæ seen in carmine or hæmatoxylin stained sections of the cerebellum are the tangential fibres to which the axis-cylinder processes of the "granules" give rise, by their division, in the form of a T or a Y. This T-division was first described by Ramón y Cajal, and has been observed in a large number of animals by Pedro Ramón. In many of my own preparations, the delicate axis-cylinder is to be seen commencing in the granule, passing between the cells of Purkinje, and divaricating in the molecular layer. It is important to notice that the branching system of Purkinje-cells, and of the "molecular" cells are arranged at right angles to the folia, the longitudinal fibrils in the direction of their long axes.

This brings us back to the old view as to the plan of structure of the cortex cerebelli, first defined by Boll and often reiterated by myself and many others. Afferent fibres branch among the granules; delicate processes from the granules stream into the molecular layer between the cells of Purkinje; dividing at right angles (as demonstrated by Cajal), they are collected by the protoplasmic processes of the Purkinje-cells, from the base of each of which a neural process passes into the medullary centre. This seems to be the basis of the reflex machine—the system of primary couples—to which the bracket-like cells of the molecular layer, the collaterals of the neural processes of the cells of Purkinje, the cells of Golgi, the fusiform cells, the scattered large cells of the granular layer, and other elements, must be fitted in as our knowledge of the connections of these elements becomes more complete.

If in the cortex cerebelli a *direct continuity of structure is established from the granules to the cells of Purkinje*, a similar continuity must be looked for in the cortex cerebri, and may be expected in the central grey tube.

The fact that the silver deposit extends so short a distance along the tangential fibrils as to give to the protoplasmic process merely a "thorny" appearance, seems to

indicate that GREY MATTER CONSISTS OF TWO SUBSTANCES WHICH BEHAVE DIFFERENTLY TO THE CHROME- OR SILVER-SALT. The ending of the thorn in a knob, as well as the frequent varicosities in the course of all other delicate fibres, especially at the points at which collaterals are given off from axis-cylinder processes, indicates that the substance which reduces the silver-salt is fluid or semi-fluid. The reduction of the silver by neurogleial cells, and the frequent appearance of the deposit outside nerve cells, show, I think, that it is *not the nerve strand properly so-called, i.e., the conducting fibril*,[1] *which reacts to silver, but the fluid or semi-fluid substance—the neuroplasm—in which it is embedded.* If this hypothesis be correct, it may be applied in many ways to explain the fact that a direct continuity of heterologous nerve elements has not been observed (except by myself in the case of the cerebellum) with Golgi's method.

The chief difficulty which I see in the way of this explanation is the fact that many ependymal cells are quite as thorny as the protoplasmic processes; but this difficulty has to be faced whatever view is held as to the meaning of the thorns. No doubt the ependymal cells are constructed upon the same plan as the web which they serve to support.

It will, no doubt, be urged in opposition to my theory, that it is not only Golgi's method which seems to demonstrate the discontinuity of nerve elements; the same thing is exhibited by Ehrlich's method, which has given such admirable results in the hands of Retzius; but I maintain that this fact is confirmatory of my hypothesis. Methyl blue injected *intra vitam* acts very quickly upon the nerves, while they are in a living state. It is much more likely that the stain is taken up from the circulation by the nutritional protoplasm of the nerves than that it affects the conducting fibrils.

The fact that NO THORNS ARE TO BE SEEN WHEN THE BRAIN IS INJECTED WITH BICHROMATE shows that the outward spread of the neuroplasm along the nerve-fibrils occurs *post-mortem*. We should, therefore, expect that Ehrlich's

[1] The question as to whether the fibrils are solid (Schultze) or hollow tubules (Nansen, Schäfer) does not affect the theory.

method would show the nerve-elements as still more discrete than they seem to be when prepared in the ordinary way by the chrome-silver method after death.

Lastly, I submit that even from the point of view of those who work chiefly with Golgi's method, it is a bold assumption that this method shows us the ultimate termination of nerve-fibrils. Speaking for myself I may say that the thought which a good Golgi-preparation of the spinal cord suggests is not, how complete the picture, but how much there must be that one does not see! The amazing delicacy of the last divisions of the collaterals impresses upon one's mind the fact that it is hopeless to try to follow them to their termination since the method is incapable of showing their ultimate subdivisions.

Still more forcibly is the inadequacy of the method brought out by a study of the cortex cerebri. Every here and there (especially when the tissue has remained a long time—say six weeks—in bichromate and osmic) occur masses of fibrils—looking like the mycelium of a fungus. The centre of the mass is an impenetrable tangle, and only at its margin can the separate fibrils be seen; it brings home to one the fact that admirable and diagrammatic as are the partial pictures, they give a very incomplete and inadequate representation of the infinitely complex tissue of the brain.

*Granules.*—Perhaps the greatest service which Golgi's method has rendered to histology is in giving us accurate information with regard to the nature and form of these minute nerve cells. All attempts to isolate the granules by teasing had failed; fragments only of their processes remained attached to the cell-body. Owing to the closeness with which they are massed together there was no hope of our being able to make out their form by studying them in sections. The chrome-silver method came to our rescue; picked out one granule in a hundred and depicted it with diagrammatic simplicity.

Since our knowledge of the granules commences with the introduction of Golgi's method, it is superfluous to quote the views of observers who had not this means of observation at their disposal. Granules were called myelocytes, connec-

FIG. 17

Adult cat; olfactory bulb. At the bottom of the photograph are seen the glomeruli. The mitral cells are very imperfectly coloured. Above the mitrals is seen a single cell of the type for which I suggest the name "bracket-cells." Its protoplasmic processes extend horizontally for more than 3 mm. Its axis-cylinder was centripetal. Numerous granules are seen above this.

FIG. 18.

Kitten, 3 days old; olfactory bulb. Showing mitral cells and the extremely thorny protoplasmic processes of the granules.

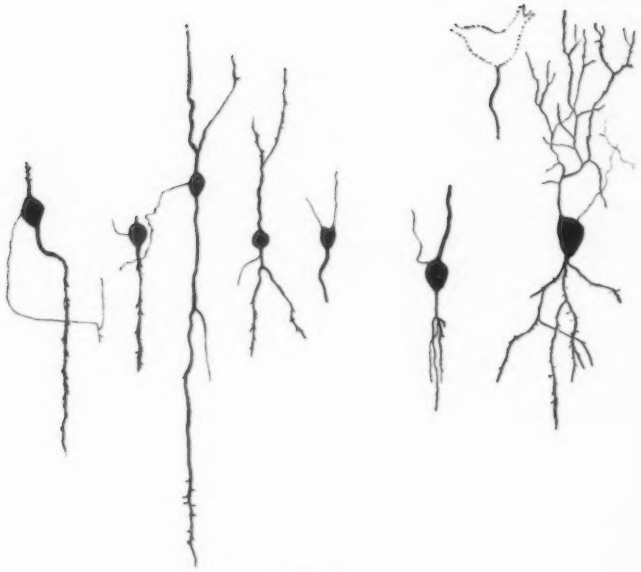

FIG. 19

Olfactory bulb; granules with axis-cylinders selected from various preparations:

1-4. Hedgehog (9 $\mu$ to 11 $\mu$).

5. Kitten, 3 days old (10 $\mu$).

6, 7. Rat, 12 days old (12 $\mu$ and 15 $\mu$).

*By an oversight* 1, 2, 3 *and* 4 *are drawn with their central ends upwards;* 5, 6 *and* 7 *with their central ends downwards.*

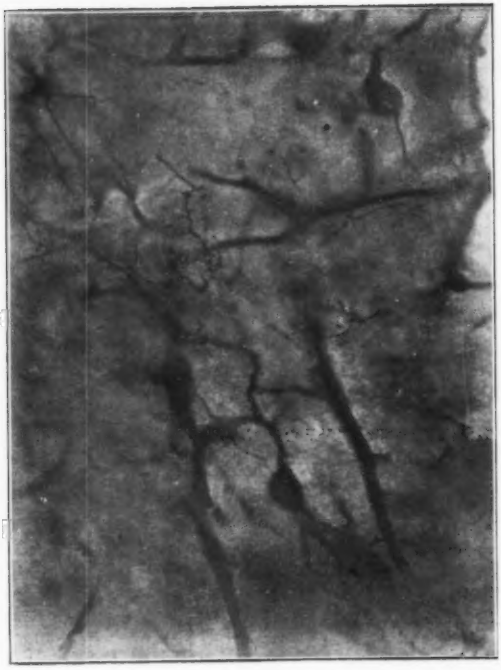

FIG. 20

Photograph of the granule 19, 7 (reversed).

tive tissue corpuscles, lymph-corpuscles, "doubtfully nervous" elements, and so forth, by men who would be the first to acknowledge that their nervous nature is now placed beyond any possibility of doubt. It is a little strange to find the hypothesis put forward in a recent memoire that they are nerve-cells which have remained behind in an embryonic condition.[1]

There are four situations in which granules are found in dense masses: (1) the olfactory bulb; (2) the retina; (3) ? the fascia dentata; (4) the cerebellum. They are very numerous in the occipital region of the cortex cerebri. That all these small nerve cells bear a similar relation to afferent fibres is not improbable; but whether on this account they should all be described as homologous is a question which cannot be answered until we have further information. In the cerebellum the granules are arranged about clumps of molecular substance (figs. 3 and 13). So far as we can see, they are all of one kind, but Denissenko[2] thought that he could distinguish a second type of nucleus by the use of eosin. I have never been able to find these eosinphile nuclei of Denissenko, although I see in the centre of each clump of molecular substance the structures which he mistook, as I think, for nuclei. These structures are usually smaller than the nuclei, homogeneous and pale; sometimes single, and round, they often appear as rods, and very frequently they are divided into several parts (fig. 3).

When I first observed these structures in sections stained with eosin, or better still with the alum-carmine-Weigert

[1] Chatin, "Études d'histologie Zoologique sur la forme dite Myélocyte," Paris, 1890.

I am not quite sure that I have given a fair representation of Chatin's views. The following quotations show that Chatin looks upon the granules as identical with the large nerve cells when in an embryonic stage; but he does not state explicitly that either the granules are capable of growing into larger cells, or that they are larger cells which have remained in an embryonic, and therefore functionless, condition. "Ce qui mérite d'être noté, c'est l'identité morphologique qui se manifeste constamment entre tous ces jeunes éléments nerveux, quelle que soit l'espèce animale sur laquelle on en suit l'évolution." "Il ne suffit pas d'avoir montré l'exacte signification du myélocyte, il faut encore établir qu'il ne peut aucunement représenter un type distinct."

[2] "Zur Frage über den Bau der Kleinhirnrinde bei verschiedenen Klassen von Wirbelthieren," *Archiv. fur Mikr. Anat.*, Bd. xiv., 1877, p. 203.

method, I concluded that they were not nuclei, but did not like to hazard the suggestion that they were, as I thought them to be, swollen axis-cylinder processes at their points of division. The use of the chrome-silver method shows, however, that this is really the case. They are the dilated fibres of the rosettes which occur on the course of Ramón y Cajal's mossy fibres (fibras musgosas).

The granules arranged around each molecular clump give protoplasmic processes to it (as well as to three, four, five, or even six other clumps). Their protoplasmic processes end in curious bent claws which are in relation with the processes of the rosette. Whether this connection is one of contact only or of direct continuity remains to be proved.

If we neglect for a moment the nuclei which have been supposed to occur within the molecular clumps, and eliminate, of course, the nuclei of the superficial "Golgi cells" and the scattered large cells, we have to deal with a vast number of apparently similar nuclei. The question arises: Are all these of one kind? The way in which the chrome-silver method picks one granule out of several hundred, is more remarkable even than its capricious selection of other kinds of cells; I have never seen the granules of the cerebellum stained in masses, as often occurs in the olfactory bulb. They are always disposed at fairly regular intervals. All observers who have worked hitherto with the chrome-silver method have concluded that only the type of granule with centrifugal axis-cylinder is present. I shall show in a moment that granules of quite different form with centripetal axis-cylinders are also to be found.

In addition to its short protoplasmic processes already described, each granule (of type 1) has a single axis-cylinder process of exquisite delicacy which makes its way into the molecular layer and ends, as Ramón y Cajal discovered, by dividing at right angles to the planes of the Purkinje-systems.

The enormous number of radial fibrils which in some sections are seen making their way to the molecular layer between the cells of Purkinje as well as the equally numerous tangential fibres found in the molecular layer in other

sections, evidently require a vast number of granules to give them origin.

### Granules with Centripetal Axis-cylinders.

It is late in the day to describe a new kind of cell in the cerebellum, but it is a curious proof of the caprice of the chrome-silver method that these granules should not have shown themselves to other observers. In one set of preparations from a four-day rat, they occur in large clusters about the apices of the convolutions. I have not yet had time to look for them in other subjects.

These new granules are quite unlike any hitherto described, nor can they be confused with the fusiform cells described by Golgi. Golgi's cells are much larger (20 $\mu$), with long protoplasmic processes from each end of the spindle, and a fibre attached to the side of the cell. The new granules have a transverse diameter of 9-12 $\mu$. From the apex, a branching protoplasmic process runs towards the periphery (figs. 14, 15), while an axis-cylinder process is attached to the base. The axis-cylinder frequently gives off a recurrent branch near the granule, and passes on towards the white matter where or near which it divides.

What are the *central connections of the granules?*

From the medullary substance of the *arbor vitæ* a single medullated nerve fibre traverses the granular layer to reach each Purkinje cell; but there can be no doubt that many fibres are left over after all the Purkinje cells are provided for. Amongst these are the mossy or rosette fibres, which form an extremely complicated and delicate branching system among the granules. In animals in which the medullary fibres separate the granular layer from the cells of Purkinje, some fibres turn towards the molecular layer, whilst others turn towards the granules. This is seen especially well in cartilaginous fishes and in some reptiles, for example, the crocodile. The fibres which turn towards the granules divide frequently, and it is on this account, probably, that there is a marked difference in size between the fibres near the cells of Purkinje and those near the granules. The former are much the larger.

Ramón y Cajal has assigned to the granules with centrifugal fibres their proper position as elements on the ascending limbs of the cerebellar reflex arcs.

The *granules of the olfactory bulb* have not been treated with so much respect as those of the cerebellum. Many considerations show us that the granules of the bulb cannot be regarded as strictly homologous with the granules of the cortex cerebelli or cortex cerebri. The organ in which they are found is widely dissimilar from the cortex, homologous with a peripheral nervous organ—the retina—and not with a central or secondary nerve field.

Nevertheless, the granules of the olfactory bulb (figs. 16, 17, 18, 19) have sufficient in common with the granules of the cerebellum to entitle them to the full status and privileges of nerve cells. To simplify the diagram of the olfactory bulb by leaving out the granules, as v. Gehuchten has done,[1] is to complicate matters for future generations of histologists:—"Les cellules mitrales sont donc les véritables cellules olfactives du bulbe. Loin d'être, comme Golgi le croit, une voie de transmission accessoire, elles forment l'unique route par laquelle l'ébranlement nerveux d'une fibrille olfactive peut être sûrement conduit jusqu'au cerveau."[2] This seems a little hard upon the granules, not to mention various other kinds of nerve-cell, which together play a much larger part in the formation of the olfactory bulb than do the mitral cells!

The granules of the olfactory bulb usually appear as minute round, fusiform or triangular cells with one very long peripheral process, which passes through the layer of mitral cells, and often approaches very near to the glomeruli, and three or four much more delicate central or basal processes which are often coloured only for a short distance. Occasionally the central processes are long and branch frequently. Sometimes the round cell-body lies on the side of a process which then extends for a long distance centrally as well as peripherally. It is rather remarkable that the peripheral

[1] *Cf.* Van Gehuchten, "Système Nerveux de l'homme," Lierre, 1893, figs. 390-393.

[2] V. Gehuchten and Martin, *La Cellule*, vii., 1891, p. 232.

process is stained much more easily than the central processes.

Both peripheral and basal processes are thorny (fig. 18); the thorns on the sub-divisions of the peripheral process, after it has passed the layer of mitral cells and entered the stratum gelatinosum of Lockhart Clarke, are remarkably long (6-12 $\mu$).

Golgi is doubtful as to the nervous nature of these cells, although he thought he saw in certain rare cases an axis-cylinder process which gave off collaterals and joined bundles of nerve fibres; as did also its collaterals.[1]

Ramón y Cajal failed to find any axis-cylinder processes, but he nevertheless considers that the form of the cells and the termination of their apical processes in close relation with the protoplasmic processes of the mitral cells justify us in considering the granules as nervous. He homologises them with the "spongioblasts" of the retina as amacrine cells—*i.e.*, cells destitute of axis-cylinder processes.

V. Gehuchten and Martin, on the other hand, consider that since the granules have no axis-cylinder processes they are not nervous: "Du moment que, à l'exemple de Ramón y Cajal, on est disposé à ne tenir aucun compte de la présence ou de l'absence d'un prolongement nerveux pour déterminer le nature spéciale d'un élément des centres, on perd par le fait même tout motif pour ne pas considérer comme étant de nature nerveuse non seulement les cellules épendymaires . . . mais aussi un grand nombre de cellules de neuroglie."

I should have thought with Ramón y Cajal that the general appearance and disposition of the granules of the olfactory bulb sufficiently testify to their nervous nature; although the presence of an axis-cylinder may be needed to place it beyond a doubt. For the axis-cylinder I have sought very carefully in a large number of different prepara-

[1] Golgi ("Untersuchungen über den feineren Bau des Centralen und peripherischen Nervensystems"; German translation, Jena, 1894, p. 52) says: "Ob auch ein anderer, nervöser Fortsatz besteht, Kann ich nicht sagen. Allerdings habe ich in einigen Fällen beobachtet, dass einer der Fortsätze, welcher gewöhnlich *aus dem Mittleren Theile der Basis der Pyramide entspringt*, etwas homogener aussieht, als die anderen . . . . . ."

tions, with the result that I can almost always find it in the case of a certain number of the granules in any given section of the olfactory bulb (fig. 19).

The axis-cylinder is a short curved process attached to the side of the granule. As it leaves the granule it twists among the other granules which are densely packed together, and is soon lost to view. I have failed to determine its further course, although I notice that it inclines towards the periphery, but I would call attention to the fact that the tissue which separates the plates of granules is occupied by a dense feltwork of fibres; some derived from the basal protoplasmic processes of the granules, but the rest distinguished by the extreme delicacy which is characteristic of axis-cylinders and their collaterals. Occasionally the axis-cylinder process divides at right angles, very near the cell, one division running centrally, and the other peripherally.

Solitary granules are to be found at the margin of the special layer of the olfactory bulb which contains mitral cells and glomeruli. Their axis-cylinder processes may be followed for some distance, but I have not succeeded in ascertaining their destination.

Fig. 20 shows the axis-cylinder process of a cell of the olfactory bulb of a twelve-day old rat: but I am not certain whether this cell ought to be regarded as a granule. It lay at some little distance from the sheet of mitral cells, giving protoplasmic processes in each direction; those which approached the mitral cells being richly branched. Its axis-cylinder process *ran peripherally* and could be followed almost up to the mitral cell layer. The cell was about half as large again as the ordinary granules, and yet I think that the disposition of its protoplasmic processes and the course of its axis-cylinder process entitled it to be classed with them. It is worthy of note that the axis-cylinder processes of several other granules were distinctly visible in this preparation, and that they also curved peripherally.

If the cell I have photographed be not a granule it belongs to a kind of cell not described hitherto. It is too small for one of the multipolar cells, often of a fusiform shape, described by Golgi, who says, besides "Der nervose

Fortsatz entspringt Gewöhnlich von der nach dem Centrum gerichtelen Seite der Zelle, bisweilen auch seitlich, um sich dann nach innen umzubiegen" (*loc. cit.*).

In passing it may be noticed that I do not find any description of the immensely large "bracket-cells," which are common features, at any rate, in both cat and hedgehog. They lie on the central side of the mitral cells, and their branching processes often extend horizontally for a distance of 2 to 3 mm. (fig. 15).

The possibility of the existence in any situation of amacrine nerve cells is too wide a question for discussion here; but it does not appear to me probable that they are to be found in the olfactory bulb. The observation of Pedro Ramón[1] that the lower the animal in the vertebrate scale the less developed are the basal processes of the granules of the bulb, seems to dispose of the idea that these cells are bipolar in the sense of having protoplasmic processes for both cellulipetal and cellulifugal conduction; it makes the existence of an axis-cylinder process for cellulifugal conduction the more necessary.

As everyone knows, the overlapping plates of granules constitute the most conspicuous feature of the olfactory bulb. It seems to me impossible to doubt that they take a large and important part in the constitution of the bulb as a nervous mechanism. A diagram of the structure of the bulb from which they are omitted is not only inadequate but misleading.

Apart, however, from the question as to whether, in the case of the olfactory bulb, we can or cannot prove that the granules are nervous, I wish to claim for them, on general grounds, a much more important rôle in the nervous mechanism than has been conceded to them by any observer who has up to the present made use of the chrome-silver method.

No one now doubts the nervous nature of the granules of the cerebellum. Yet other granules which, when prepared with carmine, picrocarmine, or any other stain very closely

[1] Ramón y Cajal, "Nouvelles Idées," p. 108.

resemble the granules of the cerebellum, are either set aside as non-nervous, or ignored altogether. It is instructive to compare a carmine-stained section of the cortex cerebri with any of the pictures which have been published of the same tissue prepared with the chrome-silver method. In the chrome-silver preparations the granules are conspicuous by their absence; whereas in a carmine preparation of the occipital cortex, or of the cortex about the calcarine fissure, their importance is beyond dispute. It is greatly to be desired that some one should work out the connections of the granules of the cortex cerebri with the aid of the chrome-silver method.

*The Granules of the Fascia Dentata.*—I have tried in vain to colour these granules with silver.

It may be doubted whether there are any granules in this layer. Sala[1] omits them altogether when recording the results of his observations with the chrome-silver method; but there seem to me to be strong reasons for thinking that the greater number of the nuclei of the "granular layer" of the fascia dentata belong to granules.

The cells of this layer, when coloured with silver, very closely resemble miniature Purkinje-cells. The body is rounded or oval; from its base an axis-cylinder process passes towards the nucleus fasciæ dentatæ. Its apex gives rise to a rich branching system (fig. 21). Sala figures these cells as placed at very regular intervals, as my preparations also show them. The coloured cells lie almost exclusively on the surface of the granular layer, as if they differed in nature from the "granules" which lie below them. In my description of the fascia dentata prepared with the carmine Weigert stain[2] I state that the average numerical relation of the small pyramids to the granules is as 1 to 8. This number coincides approximately with the relation between the unstained nuclei and the stained cells in my chrome-silver preparations.

A third reason for considering the cells of the fascia

[1] *Zeitschr. f. w. Zoologie*, vol. liii., 1, p. 18.

[2] Hill, "The Hippocampus," *Phil. Trans. of the Royal Society of London*, 184, B. 1893, p. 389.

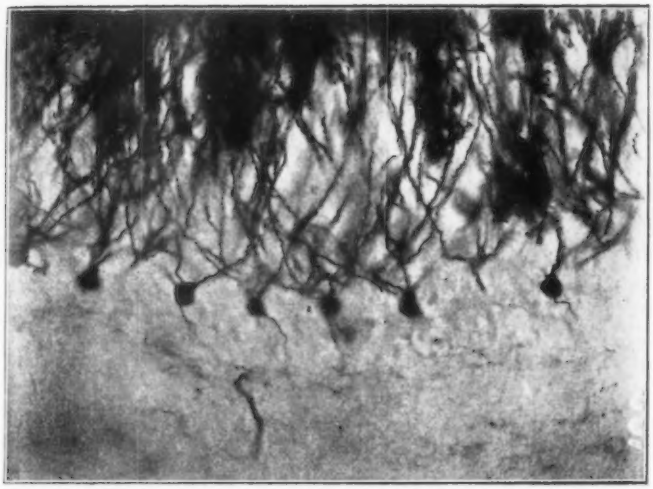

FIG. 21.
Adult hedgehog; fascia dentata hippocampi × 310.

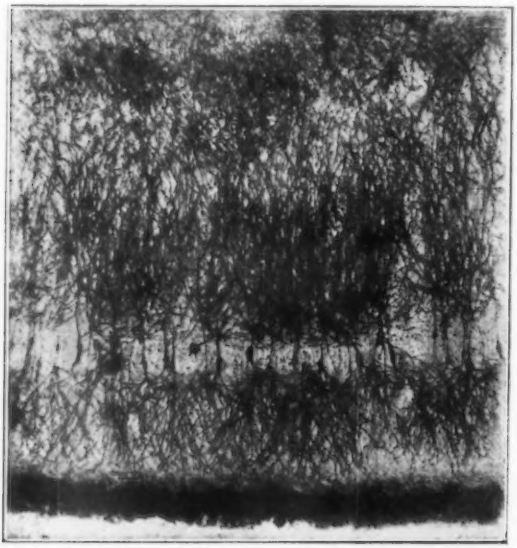

FIG. 22.
Adult hedgehog: subiculum cornu Ammonis. Showing double pyramids.

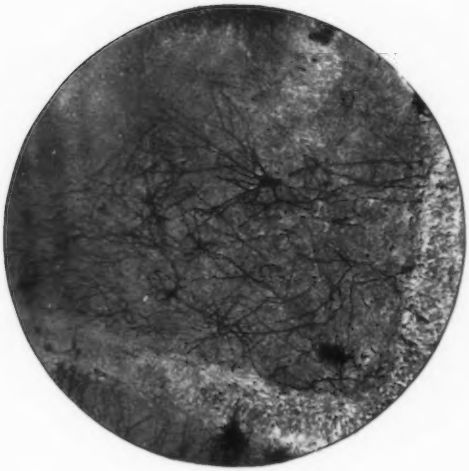

FIG. 23.

Adult hedgehog; nucleus fascial dentata × 83. Showing multi polar cells.

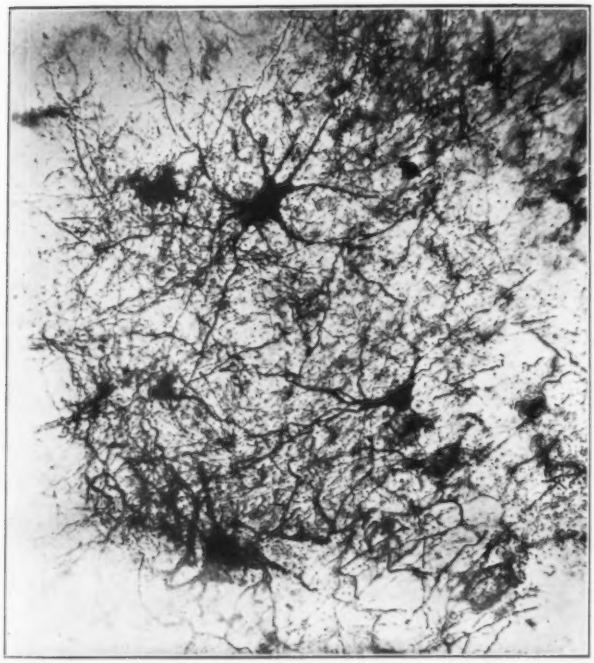

FIG. 24.

Adult hedgehog; spinal cord. Cells of the anterior horn. A single nucleus is also coloured.

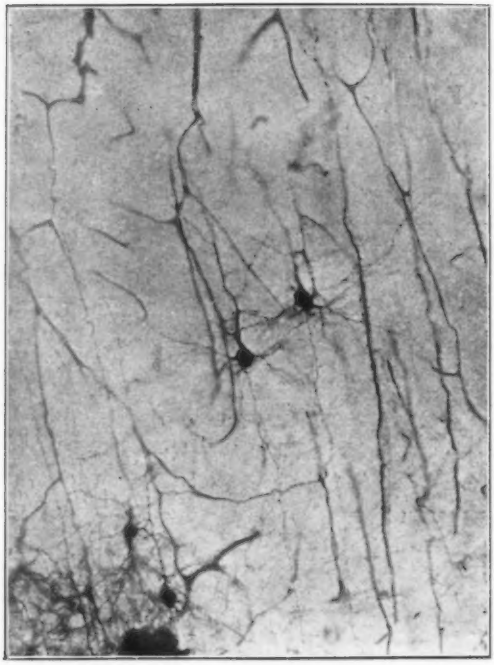

FIG. 25.

Rat, 8 days old; cortex cerebri × 155. The collaterals on the axis-cylinders of two pyramids are well seen.

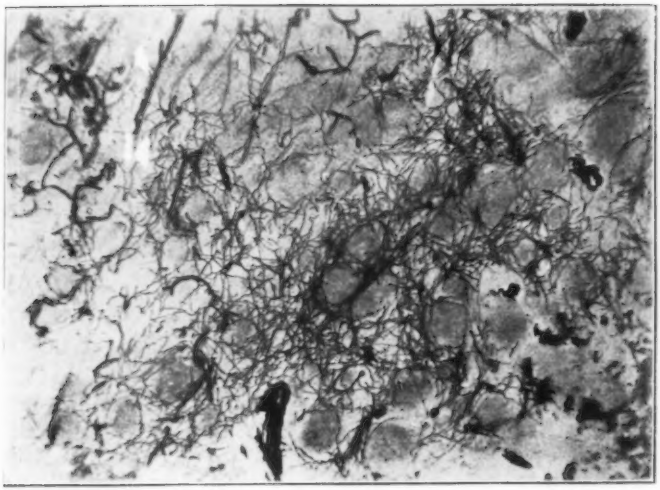

FIG. 26.

Adult hedgehog; nucleus tenticularis. The blood-vessels were injected with warm bichromate of potassium. The reaction shows cells of Golgi's type II., and also very faintly the axis-cylinders of the fibres which constitute the bundles of the internal capsule.

ALL THE PHOTOGRAPHS ARE ABSOLUTELY UNTOUCHED BY HAND.

dentata as granules is also brought out in the paper just alluded to, although its value as a proof is less obvious. The development of the fascia dentata is exactly proportional to the development of the olfactory bulb. It is conceivable that the granules in the two situations belong to the same formation.

It may not be out of place in this description of the fascia dentata to call the attention of histologists to the illustration which the hippocampus affords of the extreme difficulty of basing homologies upon the form and general appearance of nerve-cells. As the hippocampus is approached, the pyramids of the cortex cerebri give place to the remarkable "double" pyramids of the subiculum cornu Ammonis (fig. 22); at the nucleus fascia dentata these are transformed into cells, which might easily be mistaken for the motor cells of the spinal cord (fig. 23); in the fascia dentata (fig. 20) we have a type of cell for which we most easily find an analogy in the cortex cerebelli.

*Summary.*—The method of colouration introduced by Professor Golgi, of Pavia, has yielded, to those who have had the foresight to apply it persistently, an undreamed of harvest. In particular Santiago, Ramón y Cajal is to be congratulated upon the wealth of new facts which it has enabled him to discover. These are, I believe, only a first instalment of the revelations in nerve-histology which the method is destined to make.

I have used it, not with the hope of making discoveries, but with a view to ascertaining the conditions of its action and the value of its results when compared with those which other methods afford. In other words, I have tried to discover its limitations—its weakness rather than its strength.

The subject is so large, and my results so fragmentary, that I hesitate to lay them before you, and I should not, assuredly, have embodied them in their present incomplete form in a memoire. When, however, you did me the great compliment of electing me as your President, I felt that you would expect me to bring before you such results of my personal work as are likely to be of greatest interest to neurologists in general.

The chrome-silver method has completely transformed our conception of the nature of the nervous mechanism. Whatever branch of neurology we may happen to pursue, we need to lay afresh the foundation upon which it rests. The new method of colouration has revealed to us the fact that grey matter is far more complex in its structure than histologists imagined. We are also asked to throw aside all preconceived ideas as to its mode of working, and to believe that its various elements are not in structural continuity. It is on this latter point that I wish you to suspend your judgment, and in favour of my *caveat* I lodge the following considerations :—

(1) The place of the granules in the mechanism has not yet been ascertained except in the case of the cerebellum. In all cortical fields they are in intimate relation with the bulk of the ascending or afferent fibres. How close their connections with these fibres may be, still remains to be determined. Their axis-cylinder processes are also in intimate relation with the protoplasmic processes of the cells which give origin to efferent fibres.

(2) The thorns on the protoplasmic processes of nerve cells are not artifacts, nor are they, on the other hand, processes which the chrome-silver method reveals in their entirety. It is not impossible that they contain the ends of the axis-cylinder processes of the granules surrounded by an extension, or *post-mortem* overflow of the neuroplasm of the larger nerve cell.

If a direct continuity of nerve substance between axis-cylinder processes of granules and the protoplasmic processes of nerve cells be proved to exist, it may be looked for also along all other lines of impulse reflection, and Gerlach's plexus—with all the modifications in form introduced by the chrome-silver method—may be a true expression of the structure of grey matter as a nervous mechanism after all.

# ON THE INFLUENCE OF REAGENTS ON THE ELECTRICAL EXCITABILITY OF ISOLATED NERVE.

BY AUGUSTUS D. WALLER, M.D., F.R.S.

## *Syllabus.*

Introductory Remarks.

Demonstration of Representative Experiments.

*Action of Gases.*—Oxygen—Carbon Dioxide—Carbon Monoxide Hydrogen—Nitrous Oxide—Hydrogen Peroxide—Chloroform—Ether—Hydrocyanic Acid—Amyl Nitrite—Ammonia—Chlorine—Coal Gas.

Influence of Temperature—Decline and Reversal of the Currents of Injury and of Action—Effects of Alcohol and of Tobacco Smoke.

*Action of Reagents in Solution.*—Conditions of Observation—Bromide of Potassium—Chloride of Sodium—Water—Acids and Alkalies.

*Alkaloids*—Muscarin, its Case Considered in Detail with Reference to the General Method of Procedure—Nicotin—Curarin—Atropin—Cocain—Pilocarpin—Strychnin—Aconitin—Veratrin—Gelseminum—Chloral Hydrate—Butylchloral Hydrate—Antipyrin.

*Comparative Action of Haloid Salts* in Equi-molecular Solutions ($^{M}/_{10}$)—Bromides—Chlorides and Iodides of Ammonium, Sodium and Potassium—Determination of the Predominant Partner in the Molecule—Action of Calcium, Barium and Strontium—of Rubidium, Cæsium, Gold, Lithium, Copper and Zinc.

*Antagonism*, Successive and Simultaneous; False and True.

*Chloroform versus Ether Anæsthesis.*

Comparative Action on Nerve of some Ethers and Ethereal Salts ($[C_2H_5]_2O$; $C_2H_5Cl$; $C_2H_5Br$; $C_2H_5I$;

Of Chlormethanes ($CH_3Cl$; $CH_2Cl_2$; $CHCl_3$; $CCl_4$);

And of Chlorethanes ($C_2H_5Cl$; $CH_2Cl\text{-}CH_2Cl$; $CH_3\text{-}CHCl_2$; $CH_2Cl\text{-}CHCl_2$; $CH_3\text{-}CCl_3$; $CH_2Cl\text{-}CCl_3$; $CHCl_2\text{-}CHCl_2$; $CHCl_2\text{-}CCl_3$).

The experiments on the subject of the lecture, and the lecture itsel have been considerably extended during the past year, and the portion now published relates mainly to the action of anæsthetics. The accompanying illustrations, in several instances reproduced from records taken since July

6, refer only to the action of $CO_2$, chloroform and ether. Evidence relating to other substances mentioned in the text, and to the antagonism of chloroform by $CO_2$ will be presented in subsequent papers. The three principal experiments described below ($CO_2$, abolition then augmentation; $Et_2O$, temporary abolition then recovery; $CHCl_3$, permanent abolition) were demonstrated at the November meeting of the Physiological Society (Proceedings of November 9 in *Journal of Physiology*, vol. xviii., p. 45).

THE first thought that suggests itself when one has seen what a surprisingly regular series of effects is obtained from nerve by regular excitation at regular intervals, is that we are in possession of an admirable test by which to recognise the action of drugs upon the excitability of nerve, and, as we shall presently see, the surprising regularity of the normal effects is paralleled by an even more surprising regularity in the modifications of these effects, caused by drugs.

*A priori* we should not have anticipated such clear results as we shall witness; nerve, the conducting organ, is, in relation to knowledge of this order, practically a blank sheet: nerve poisons are regarded as acting only upon the central and peripheral end-organs, not upon the conductors, and with the exception of observations by Biedermann, on the effect of ether upon physiological electrotonus, no positive data exist touching this fundamental subject. As far as concerns experimental pharmacology, nerve, apart from its end-organs, does not yet exist.[1]

Yet *a priori* again, while fully admitting the superior susceptibility of terminal grey matter to the modifying action of drugs, there would seem to be every probability in favour of our finding the conducting grey matter, *i.e.*, the axis-cylinder, similarly susceptible, if in less degree.

But it is not to speculations alone that I am about to call your attention. I intend to show you that pure nerve is accessible to such experiments—that it is in fact the

[1] I do not, of course, ignore the numerous investigations upon nerve by Ranke, Kühne, Grützner and many others, in which the action of reagents upon nerve has been gauged by muscular and by sensory reactions. The statement made above refers to *isolated* nerve. The only observations relating to isolated nerve that I have been able to find in toxicological literature are those of Mommsen on the action of poisons (*Virchow's Archiv*, 1881, p. 243), inclusive of alcohol, chloroform and ether. Mommsen employed the usual nerve-muscle preparation, but also as a confirmatory test the galvanometer, thus employing nerves that were *isolated* from their end organs.

tissue above all others suited to exact investigation of the chemical action of reagents upon excitable, that is to say, living matter.

Let us begin with gases, with, say, carbon dioxide, chloroform, ether, hydrocyanic acid, &c., preferring these to drugs in solution for the obvious reason that we can most easily apply them with least disturbance to the nerve.

The disposition of things is as shown in this diagram, the parts of which need merely be named in order that their purpose may be understood. A gas-chamber with

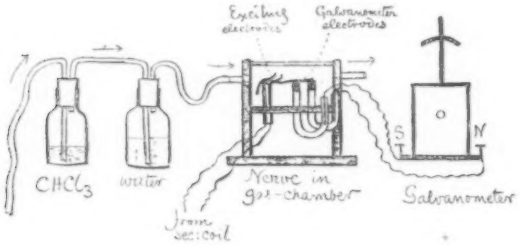


FIG. 2.

inlet and outlet, containing a frog's sciatic nerve[1] laid upon exciting and leading-off electrodes, wires from an induction

[1] Mammalian nerve is unsuitable. As was shown at a previous lecture, the negative variation vanishes rapidly from excised nerve. The statement of Hermann as to the long continuance of excitatory phenomena on rabbit's nerve *post-mortem* is correct if by excitatory phenomena electrotonic changes are signified; that of Fredericq as to the existence of a true negative variation in mammalian nerve twenty-four hours *post-mortem*, is, I think, open to question. A true negative variation—*i.e.*, one independent of distance between exciting and leading-off electrodes, and not reversed by reversal of the excitation—has never come under my observations of excised mammalian nerves; electrotonic effects have been particularly prominent; but to what extent such effects are to be admitted as physiological phenomena is an unsettled question that cannot be profitably discussed in this connection. The effects under observation are, to the best of my knowledge, true negative variations, and if to any extent an electrotonic factor has also been present, it has been a physiological phenomenon subject to the influence of excitatory and depressant drugs.

coil to the nerve, and from the nerve to the galvanograph. Two wash-bottles, one for the drug, the next for water, to avoid drying in the gas-chamber when gas is blown or sucked through it.

A couple of representative experiments carried through under your eyes, and, while the experiments are going on, the exhibition of the autographed results of other similar experiments, cannot fail to convince you that we are here in possession of a method of investigation second to no other.

For the test is applied to nerve and to nerve only. There is not, as when muscular contraction is used as the indicator, any question as to the share borne by muscle or by the motor end plate in any effect that may be produced. The isolation of the object of experiment is complete. It does not move. Mere excitation does not exhaust its excitability.

The galvanometer spot on the screen has moved southwards four times during the last four minutes, at each minute the nerve in the gas-chamber has been excited for one-eighth of a minute by completion of a tetanising current of a strength of ten units; as you saw, the successive deflections were of regular magnitude. I now blow chloroform vapour through the gas-chamber, and watch for the next excitation by closure of circuit at the mercury pool. There is no effect, nor at any succeeding closure. The excitatory effect has been abolished by chloroform while I was speaking; the nerve is completely anæsthetised. Its excitability may not, however, have finally disappeared, the nerve is not necessarily dead, for if I disconnect the chloroform bottle and blow moist air through the gas-chamber you may (or you may not) see, if you will wait, a recovery of the effects of excitation. But the reappearance, if it occurs at all, will take some little time, which we may employ upon another similar experiment.

Here is a second gas-chamber, and nerve similar to the first, upon which we will make a double-barrelled experiment, first $CO_2$ then ether, neither of which will miss fire.

The excitatory effects are as you see quite regular, between each two effects I have turned a reverser so as to reverse the direction of the exciting current in the nerve and the deflection due to the "action current" has remained unaltered. $CO_2$ gas is now passed through the gas-chamber for about a minute. During the next minute or two the deflections are suppressed, but very soon the suppression (or it might have been only diminution) makes way for an augmentation which might persist for ten, twenty or thirty minutes. But we shall not wait for this.

Ether vapour ($Et_2O$) is now passed through the gas-chamber for about a minute as before. The deflections that would otherwise have made their appearance each minute are, at any rate after the first minute, completely suppressed. They will, however, soon reappear, even though I do not as in the case of chloroform, air the chamber, they will do so in a few minutes and they may (it is not likely in this case that they will) be progressively increased to a magnitude considerably above the normal.

I do not wish to smother these main facts with details, however important the latter may seem to be, but before stopping these experiments, will prolong them for five minutes and give you in a few words the results of over a hundred similar experiments with the three reagents, $CHCl_3$, $Et_2O$ and $CO_2$.

Always the immediate effect of any of these three reagents, when strong, is an abolition of excitability, temporary in the case of $CO_2$ and ether, often final in the case of chloroform. With $CO_2$ and ether the nerve comes to without aeration of the gas chamber; I have never seen it do so with chloroform, and have often failed to bring it round by aeration. The first two reagents have a true anæsthetic, *i.e.*, temporary effect, the third is more prominently toxic, and its effect is apt to be final. The after-effect of both $CO_2$ and ether administered in abundance to the nerve is an augmentation of excitability, most prominent in the case of $CO_2$, of which, moreover, an anæsthetic period is briefer than in the case of ether.

Administered in a diluted state, *i.e.*, with much air, all

three reagents give as their immediate effect on nerve an augmentation of excitability that gradually wears off, most rapidly in the case of chloroform, of which the action on nerve is most manifestly toxic.

If time were unlimited, I might go on to show you a series of experiments upon a series of nerves put up in moist chambers, but it will be more economical, while affording you a more comprehensive survey of quietly conducted experiments, if I project their autographed records upon the screen. From the tests and precautions that you have witnessed on previous occasions, you are more or less assured that fallacies have been guarded against, and that there is no question of current escape, or of electrotonic effects, or of unipolar action, or of magnetic action of the induction coil. Moreover, the records will speak for themselves. Here are records of the effect of carbon dioxide, of carbon monoxide, of ammonia, of hydrocyanic acid, of oxygen, of ordinary coal gas, of nitrite of amyl, of hydrogen peroxide, of nitrous oxide — in short, of everything that happened to be within easy reach.

Carbon dioxide we have just studied. Carbon monoxide does nothing. Oxygen does nothing, or very little. Strong ammonia kills, weak ammonia excites. Hydrocyanic acid kills; here are two records (plates 238, 341), the first of HCN vapour as given off to the gas-chamber by blowing into it through Scheele's preparation (? 5 per cent.), the second of alcohol vapour by blowing through absolute alcohol; you could hardly distinguish them from each other. Chlorine from BP water kills; chlorine from BP water diluted twenty times, excites. Hydrogen peroxide excites. Methane excites. Hydrogen sulphide excites, then kills. Nitrous oxide does nothing; anæsthesia by laughing gas is probably anæsthesia by $CO_2$.

The effect of temperature upon nerve is equally easily tested. Here, again, we have the satisfaction of knowing that nerve and nerve only is submitted to observation. All that is necessary is to enclose our gas-chamber, nerve and electrodes in a larger box, of which the temperature can be raised and lowered at will. Such an experiment is, indeed,

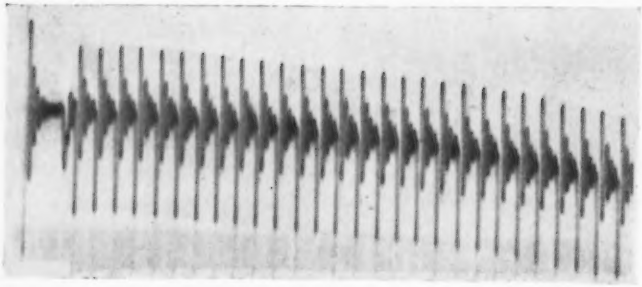

FIG. 1.

A normal series of negative variations.

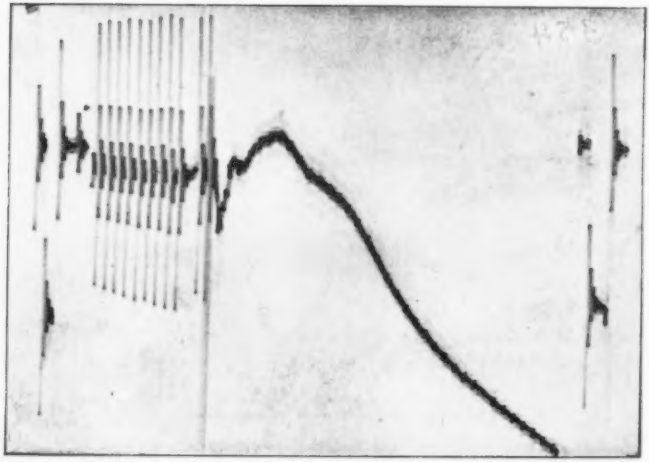

FIG. 3.

Effect of chloroform on the negative variation. Permanent abolition.

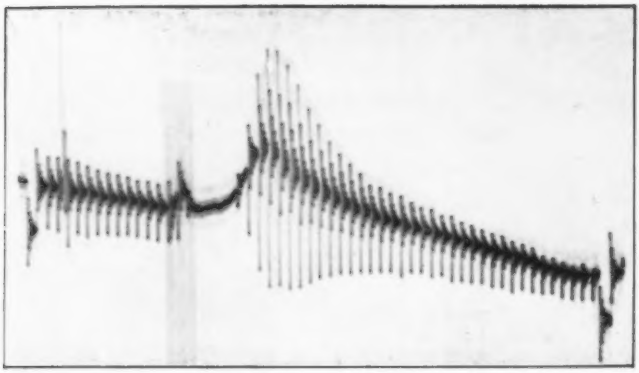

FIG. 4.

Full effect of "much" carbon dioxide on the negative variation. Temporary abolition followed by secondary augmentation.

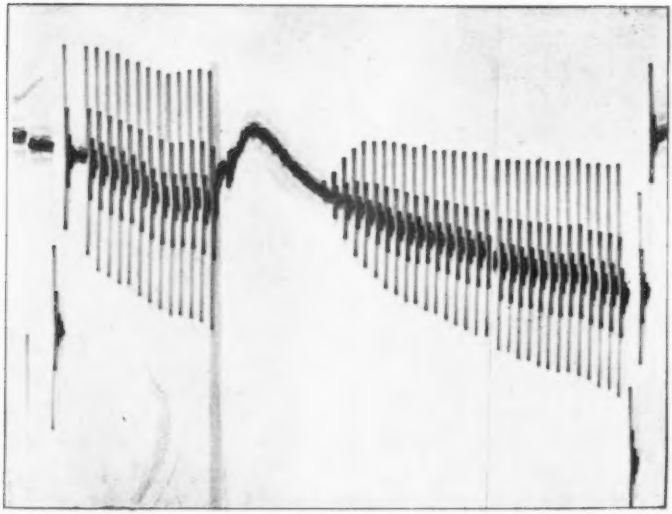

FIG. 5.

Full effect of ether on the negative variation. Temporary abolition followed by recovery.

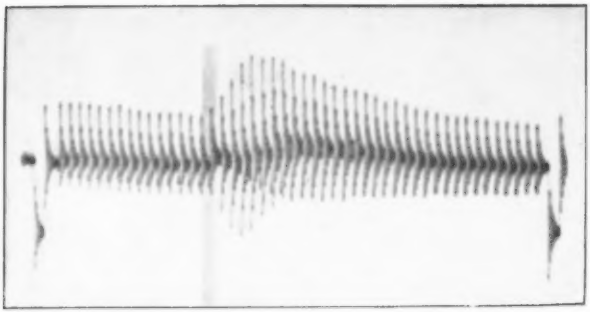

FIG. 6.

Effect of dilute chloroform vapour. Primary augmentation.

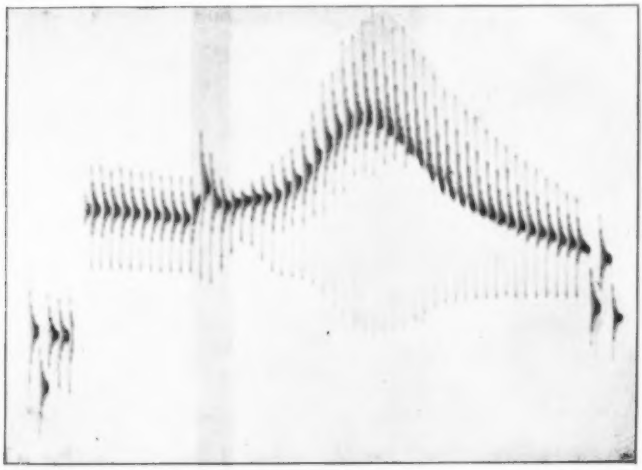

FIG. 7.

Effect of "little" carbon dioxide. Primary augmentation followed by secondary augmentation, separated by a short intervening period during which there is apparently a struggle between augmentation by "little" $CO_2$ and diminution by "much" $CO_2$.

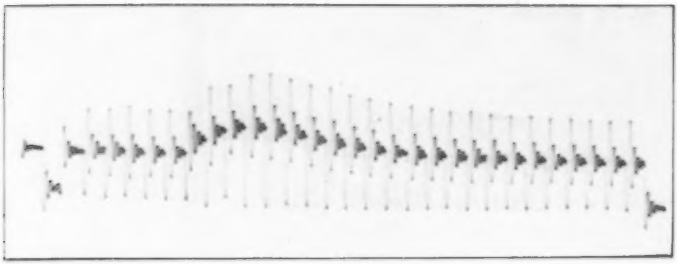

FIG. 8.

Slight effect of ether. Primary augmentation.

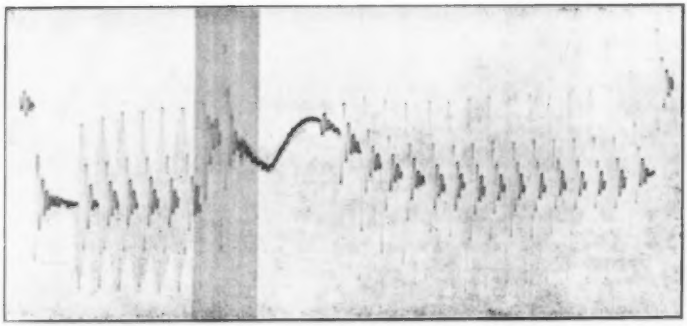

FIG. 9.

Full effect of ether on the same nerve. Primary temporary abolition followed by recovery.

a natural preliminary to any others, for we require to know before testing any gradual effect, what is the gradual effect of temperature alone; what, *e.g.*, may be the difference of effect according as tests are made in summer or winter, at—say 20° or at 5°.

It was indeed an apparently regular difference between my winter and my summer results at these two temperatures respectively, that first made me examine this presumable influence of temperature, for whereas at 5° an almost regular or only slightly diminishing series was the rule, at 20° the series always exhibited more or less decline; nerves were far more enduring during January and February than during July and August, which, indeed, is not matter for surprise.

Experimental raising of temperature (from an initial temperature of 20°) caused a diminution progressing to abolition as the temperature reached 35° to 40°. The nerve was not killed at this last named temperature, for with the subsequent fall to 25° and 20° the variation returned and reached to about three-fourths of its original value.

There are of course many other possible causes of an inconveniently rapid decline—diminution in the strength of the exciting current, which we have tested and found not to diminish under even more severe trial; drying of the nerve, which we have counteracted by the moist chamber; the natural decline of the injury-current, which we have as far as possible escaped by waiting until the current was declining sufficiently slowly;[1] alterations of resistance, which we have

[1] I found later that an excellent means of obtaining a level series of regular effects is afforded by the calcium salts; a one minute bath of a decimolecular solution of $Ca\ Cl_2 \cdot 2H_2O$ (0·147 per cent.) or preferably in $Sr\ Cl_2 \cdot 6H_2O$ (0.266 per cent.) secures this often very desirable result. First trials are of course made with a normal nerve, subsequent trials on descending and ascending series induced by a potassium and a calcium bath respectively. A steady and uniform run is of course the most favourable condition of any sort of test, but failing this, it is preferable to test an anæsthetic, or other depressant reagent upon an increasing deflection, a reviving or stimulant reagent upon a diminishing deflection. To the former of these two conditions, strontium chloride was of most welcome assistance, increasing to a steady run the otherwise unworkably declining effects given by the nerves of even the most miserable little frogs. Later still—after I had found that a rapidly declining series was significant of a previous $CO_2$ effect—I omitted the strontium bath, removed the nerves immediately after decapitation, and placed them until wanted in a decimolecular solution of NaCl.

controlled by graduation; acidity of the clay electrodes, an accident that has occurred to us, but ought not to occur again; diffusion of sulphate of zinc through the saline clay to the nerve, which we have practically escaped, by a very long clay plug and by not using the same electrodes for more than one experiment. Finally—and this indeed turned out to be the most essential condition of all—nerves left for any time subject to the reducing action of living tissues, regularly give declining series, this being, as will be shown later, a characteristic effect of $CO_2$.

Since the galvanometer is an indicator of *current*, and since current depends upon two factors—electromotive pressure and resistance—it is clear that we must adopt means of determining what alteration, if any, the resistance of our nerve has undergone before we may draw inferences as to alteration of its electromotivity. We shall effect this by a very simple application of Ohm's law, which will afford us incidentally one more justification for a clear understanding of that fundamental physical principle.

Here is an extreme case illustrating the effect of an augmentation of resistance in contributing to a diminishing current of injury and a diminishing excitatory deflection. I give it principally in order to insist upon the necessity of taking a standard deflection before and after each observation.

| | At outset. | | One hour later. |
|---|---|---|---|
| Current of injury .. .. .. | 40 | Current of injury .. | 15 |
| Negative deflection by 10 units .. | 10 | Negative deflection .. | 3 |
| Standard deflection by 0·001 volt .. | 10 | Standard deflection .. | 5 |

*i.e.*, the resistance was doubled, halving the effect of any given P.D.; if the P.D. of the currents of injury and of action had not declined, their deflections at the end of the hour with doubled resistance should have been 20 and 5 respectively. As it was they were 15 and 3, viz., a fall of 25 and of 40 per cent. respectively. Except as an illustration of the resistance fallacy the experiment is of no value.

This little resistance box, arranged on the principle of a rheochord, but with a much higher resistance so as to swamp

any alterations of resistance of the cell, delivers to the nerve-galvanometer circuit the pressure of $\frac{1}{1000}$ volt, the deflection of which, recorded at beginning and end of an observation by means of a suitable key, shows whether the resistance of the circuit is high or low, altered or unaltered. If the resistance has diminished during an experiment, the standard deflection will be greater at its end than at its beginning, and *vice versa* if the resistance has increased.

The diminution of the variation by heat is very obviously accompanied by an alteration of the zero value, the line of departure goes north then south. But I place no significance upon this alteration of zero by temperature, for a similar alteration occurs in dummy experiments with a wet thread instead of the nerve, laid upon the leading-off electrodes. I have not experimentally analysed the change into its physical and physiological factors, and have no idea how much mere alterations of resistance contribute to the effect.

I do not, however, mean to imply that in all cases the alteration of zero is to be regarded as insignificant, but that I am not able to perfectly distinguish between an alteration of zero due to a physical modification of the electrodes and an alteration due to a physiological modification of the nerve. That the latter is really in cause is unmistakably proved by a variety of features, among which these are the most noteworthy.

(1) In all the plates, without exception, the inclination of the base line as time went by is from north to south (transverse section of nerve to N. terminal); this decline, steep at the outset and running on concave to the abscissa, has been due to the well-known progressive fall of the current of injury.

(2) On review of the plates exhibiting for a sufficient length of time the effect of a "stimulant" or of a "sedative" drug, it is noticeable that stimulant effects exhibit (in addition to the augmented rhythmic excitatory deflections which have been the principal subject of our attention) an inclination of the base line from south to north, *i.e.*, in the direction of an increased current of injury, while depressant

effects exhibit an inclination from north to south, *i.e.*, in the direction of a diminished current of injury.[1]

In prolonged experiments the declining deflection may fall to nothing and then gradually increase in a reversed direction. Without having specially studied this matter I have, in several instances, found this reversal to be attendant upon a reversal of the current of injury. From a theoretical standpoint this should *invariably* be the case; nevertheless, I can remember instances in which the deflection was reversed (viz., north) when the injury current appeared not to be reversed (viz., north of the zero). It is very probable that the decline and reversal of the current of action and the decline and reversal of the current of injury are associated phenomena, dependent upon the act of death gradually progressing in the nerve. Dying tissue is chemically more active than and electrically negative to either normally living or completely dead tissue; at the outset of an experiment, transverse is more dying than, and therefore electrically negative to longitudinal contact, the current of injury is north, and the current of action south; later on when transverse is dead and longitudinal dying, longitudinal is negative, more dying than and therefore electrically negative to transverse, the current of injury is south and the current of action north. But, however this may be, whether this be the correct interpretation or no,[2] the direction of the currents of action and of injury are immaterial as regards our present purpose. I have not a very large number of observations taken upon a reversed deflection, viz., only ten out of a total of between 400 and 500, for I did not often make tests upon what was to be regarded as a stale nerve, still among these ten I find recorded some of the most characteristic effects—of ether and of chloroform and of strontium namely.

[1] Of the plates here reproduced, fig. 4 best illustrates the augmentation of current, fig. 3, its depression. The two statements made above refer to currents of normal direction.

[2] Further observations have convinced me that this interpretation is not correct, and that a reversed deflection is independent of a reversed current of injury. Whether it is a true positive variation of the same order as the negative variation of du Bois-Reymond and the positive after-variation of Hering, or an anelectrotonic current aroused by faradisation, must for the present be left open. Whatever its mechanism may be, it is subject to the action of anæsthetics, and therefore presumably a physiological effect.

I should add that my natural prejudice against stale nerve has of late very much diminished. Here is an extreme case of the sort of experience that has had this effect. (Plate, No. 435-6-7.)

FROG KILLED EIGHTEEN HOURS PREVIOUSLY, KEPT IN A MOIST SPACE.

| | Deflection. |
|---|---|
| At outset of observation .. .. .. | — 3·5 mm. (·001 volt = 20 mm.) |
| Ten minutes after bath of $^{m}/_{10}$ Sr $Cl_2$ for one minute .. .. .. | — 3·5 to — 7·5 |
| Ten minutes after second bath .. .. | — 23 |
| Twenty minutes after second bath .. | — 39 |
| Chloroethylene chloride $CH_2Cl.\ CHCl_2$ vapour for one minute .. .. | 0 |
| Thirty minutes later .. .. .. | — 6 |
| $CO_2$ for one minute .. .. .. | 0 |
| Five minutes later .. .. .. | — 9 |
| Thirty minutes later .. .. .. | — 4 |

It is advisable to use a new gas-chamber and electrodes for each separate experiment with volatile drugs. I mention this point partly as a practical hint, partly in proof of the extreme susceptibility of this method of testing. Using a moist chamber that had been used the day before for a chloroform experiment, on another occasion using one that had been used an hour before for an ammonia experiment, I found that the excitability of the nerve underwent a more or less rapid decline, giving nothing like a normal series such as shown in fig. 1. And in early experiments with solutions I had similar experiences—with potassium salts in particular, also with bromide of gold, and with cocain. So that the comparatively slight recovery that may often occur when a toxic gas, chloroform and hydrocyanic acid in particular, is blown out of the chamber with air is hardly surprising. Another point may be mentioned as being illustrative of the great delicacy of the test. At first I used to clear out the experimental gas sometimes by blowing at the inlet, sometimes by sucking at the outlet, but I soon noticed that the first proceeding was generally more effectual than the second, a result that is intelligible enough when we have witnessed the surprising effect of $CO_2$; by blowing into the gas-chamber, expired air with, say, 4 per cent. $CO_2$, was sent in; with sucking, atmospheric air was drawn in. And I

can illustrate this difference to be a reality by an actual example chosen from among many. We may well pause to admire the precision with which the isolated nerve has responded to the chemical difference between atmospheric and expired air, and—what is, perhaps, more immediately to the point—to fit an ordinary india-rubber spray-ball to the inlet of the gas-chamber.

If you wish to promptly and temporarily abolish a large effect, use ether, and use it as freely as you like, the effect will still be temporary. If you wish to instantly and permanently abolish a large effect the best card to play is chloroform. A few puffs of tobacco smoke are probably the readiest means of temporarily augmenting a small variation, or a few bubbles of $CO_2$, if the apparatus is at hand, will be even more effective. Always so—in, I may now say, scores of trials *I have never had one failure*, which anyone with recollections of experimental accidents will admit to be a strong statement to make. The augmentation is not however anything like as permanent as the augmentation we shall witness as the result of calcium or strontium; moreover, as indeed you may remember from plate 633 (fig. 4), the augmentation may be secondary to a primary diminution or abolition. It is, in short, a question of quantity, little $CO_2$ gives primary augmentation, much $CO_2$ gives primary diminution and secondary augmentation; in any case, augmentation is the salient character of the $CO_2$ effect.

At first thought, especially in remembrance of Grünhagen's experiment, in which the direct excitability of nerve is abolished by $CO_2$, this secondary nerve-reviving effect of $CO_2$ is rather surprising. Yet our surprise grows less on second thought, especially if we should happen to recollect the drift of Brown-Séquard's admirable but now almost forgotten "rouge et noir" research.[1] $CO_2$ excites nerve centres; venous blood, or a plus of $CO_2$ in inspired air causes an immediate increase of respiration, quite apart

[1] Brown-Séquard, "Recherches expérimentales sur les propriétés physiologiques et les usages du sang rouge et du sang noir et de leurs principaux éléments gazeux, l'oxygène et l'acide carbonique," *Journal de la Physiologie*, i., 1858. *Comptes Rendus de l'Académie des Sciences*, xlv., 1857.

from the effect of an oxygen deficit; soda-water is a very common ingredient of restorative drinks; champagne is more exhilarating than hock. You may think that the restorative effect on the human subject of, say, soda-water is in many cases due to the presence of brandy. Admitted, but brandy-and-soda is a more effective stimulant than brandy-and-water.

The next drug to test is obviously alcohol. What will the nerve say to alcohol vapour, or to a mixture of alcohol vapour and $CO_2$? Let us pass alcohol vapour or $CO_2$ through a wash-bottle with some brandy in it, and see what happens. The nerve approves, if signs of increased excitability be signs of approval: there certainly is an effect, reminding us of exhilaration on the human subject. As in the case of ordinary man, then, the excitability of an isolated nerve is raised by $CO_2$ by alcohol and by tobacco smoke.

Pray do not imagine that I am offering any plea for (or against) the use of alcohol and tobacco: my business is merely to observe and compare phenomena *inter se*. Besides, here again the question of quantity in relation to excitability comes in; I might put side by side plates of alcohol and of calcium phosphate to plead for alcohol, and plates of alcohol and hydrocyanic acid to plead against alcohol. Here they are, but notice the alcohol strengths—10 per cent. in the "evidence" for alcohol, absolute in "evidence" against alcohol.

Do not let me, however, be taken as urging to extremity a comparison between the properties of an isolated nerve and those of a human organism. Obviously a nicely-adjusted organism, with organs of many grades of susceptibility, including nerve centres of the highest susceptibility, is not adequately represented by a single tissue, such as nerve, which, as we have seen, tolerates interruptions of blood supply and holds out against wear and tear to almost incredible extremities. Clearly the excitabilities of a man's nerve centres may not be taken as represented in miniature by the excitability of a frog's nerve. We may study on parallel lines the comparative efficacy of such drugs as

alcohol, chloroform, ether on the living organism and upon the living tissue, and from their scale of action on the latter draw conclusions as to their scale of action on the former, but we may not pass from one line to the other and conclude that because nerve tolerates a given poison, a man's nervous system will equally tolerate that poison; we may not, for instance, argue that because a nerve will go on without blood and without oxygen, a man will be similarly independent. All we may do is to conclude from the action on nerve to a similar action on the nervous system, and to argue from the differential action of two drugs upon living nerve to a similar differential action on living man; the scale of quantity and time may be, and most probably is, very different from that on which our nerve data have been observed. Take $CO_2$, for example, we find that in small quantity it raises excitability, that in large quantity it depresses, then raises excitability in the case of nerve; we may fairly infer that it will have similar effects upon the nervous system of a man, effects that will declare themselves in the parts of greatest susceptibility; but we may not conclude that a man will tolerate $CO_2$ in quantity or for periods that are found to hold in the case of nerve. Take $N_2O$ again; we find that, as compared with $CO_2$, it has no action on nerve, we may conclude that on man it has, at any rate, less action on the nervous system than has $CO_2$. Take ether and chloroform; we find on nerve that the latter is far more toxic than the former, we may infer that a similar difference will obtain on man. And having traced a parallelism in cases well known such as these, we may proceed further, and, in the case of a drug of unknown or of doubtful action, use a nerve test as at least a preliminary question—and—answer in exact terms pointing the way. Find an antagonist to chloroform on a frog's nerve, and you will in all probability have found an antagonist to chloroform on a man's nervous system. Do not either mistake the nature of the argument, as, for instance, by taking the action of chloroform on excited nerve as an evidence that chloroform anæsthesia is due to an action on a man's intact nerves; chloroform acts upon all living matter—upon vegetable as

well as upon animal protoplasm; when a man is chloroformed, chloroform acts upon all his tissues, but takes effect by virtue of its action upon his most susceptible parts—upon his highest nerve centres first, then his lower centres, may-be his medulla, may-be his heart, and in all likelihood he is perfectly inexcitable as to his brain long before his nerves have been sensibly affected. Anything having power over nerve will have power over nerve centre, but the converse does not hold good: an alteration sufficient to excite or to paralyse a nerve centre is not necessarily sufficient to excite or paralyse a nerve.

And there are many considerations to be borne in mind in connection with any method by which drugs are brought into immediate relation with isolated tissues and organs; not as many, indeed, as under the complex conditions presented by a human organism into which a drug or a collection of drugs is experimentally poured, but still many, and among them considerations that bid us pause before transferring results of such experiment forthwith to therapeutics.

Above all, the drug is applied in a big dose and rapidly to a tissue as compared with the gradual diffusion of a much smaller dose diluted in the mass of blood, chemically altered, it may be, by the digestive fluids or by the living organs. We classify drugs as stimulant and sedative. Can you name many "sedative" drugs that do not on occasion stimulate, or one "stimulant" drug that, if pushed, does not exhaust and depress? Consider some of our best known drugs—morphia, alcohol, chloroform, ether, strychnia. Morphia a sedative, alcohol a stimulant, chloroform and ether anæsthetics, strychnia a convulsant. These are the prominent effects of the drugs respectively under their ordinary modes and conditions of exhibition to the human subject, but our knowledge of their therapeutic value could never have been a mere translation to the human subject of facts ascertained on frogs or dogs or rabbits.

I may seem to be expressing distrust of laboratory facts; that is, however, not my meaning, which is that such facts must be intelligently digested and intellectually integrated,

not merely swallowed whole in the laboratory to be served up whole at the bedside.

What we can learn as regards the action of a drug upon an isolated living, that is to say excitable, tissue is in principle whether its predominant action is to excite or to suppress activity. A drug that has any action at all on the tissue must produce one or other of these effects, and, *a priori*, might be expected to produce both effects. Most sedative drugs in the earlier stages and at lower doses are stimulant; all stimulant drugs in the later stages and at larger doses are depressant. Opium is a stimulant before it is an opiate, brandy is an opiate after it has been a stimulant.

By the direct application to nerve of any drug having action upon nerve, we may expect to witness a depressant action; and it will only be in exceptional cases or in cases where the drug is applied cautiously and gradually that we shall also witness a stimulant action. Even bromide of potassium, the predominant effect of which is depression, may be shown to produce a preliminary stimulation.

The practical rule as regards procedure towards isolated nerve seems to me to be as follows—taking for granted that the obvious precaution has been observed of applying the as far as possible *isolated* drug—namely, to observe the first smallest producible effect as well as the ultimate effect of comparatively large doses.

The latter was all we did above, and we found that the main effect in each case was depression of function, but did we go too fast with the intoxication, did we miss a preliminary stage of excitation? That can only be determined by carefully examining for the first smallest producible effect.

What we may expect to find is that any "stimulant" drug if pushed, becomes depressant, but we may also admit as reasonably probable that drugs should be encountered with an *ab initio* depressant action.

We have a familiar instance of a stimulant followed by a depressant action in the case of alcohol. Here is another instance which has occurred in one of my preliminary trials;

testing the nerve by strong ammonia, I obtained an immediate loss of excitability; testing with weak ammonia—in this instance a chloroformed nerve to see whether ammonia had any restorative action upon such a nerve—I obtained an augmentation of excitability; in fact, whereas the chloroformed nerve gave no effect, it did give a distinct effect when weak ammonia vapour was blown through the gas-chamber.

This matter of chloroform and ammonia has interests of a practical character, and I therefore repeated it more than once, varying the strength of chloroform and of ammonia, and submitting the nerve to chloroform after ammonia, or to ammonia after chloroform—or to both vapours simultaneously—with the view of bringing out the probable antagonism between them.

But more experiments are required before I may venture to make positive statements of detail on this point. All that I may legitimately do at present is to lay before you items of evidence in illustration of the stimulant and depressant action of ammonia, of chlorine, of chloroform and of ether.

Here is a plate (No. 191) exhibiting the action of "strong" ammonia vapour upon a normal nerve; the series of deflections before ammonia are quite regular, and on the plate have an amplitude of 25 mm., after ammonia they are still regular, but with an amplitude of less than 1 mm.

Here is another plate (No. 209) exhibiting the action of "weak" ammonia vapour upon a nerve completely paralysed by the previous administration of chloroform vapour.

PLATE 209.
Normal deflection = 8 mm. (regular).
Deflection after $CO_2$ = 30 mm. (regular).
Deflection after $CHCl_3$ = 0 mm.
Deflection after $NH_3$ = 5 mm. (declining).
10 minutes later = 0 mm.

As you may gather by comparing this plate with other chloroform plates, the recovery is obviously not spontaneous, but provoked by ammonia; moreover, as you see, it is not complete nor permanent. Ten minutes later the deflection has fallen again to zero. Perhaps there was too

much chloroform, perhaps there was too little ammonia. However that may have been, here is another observation in which there was certainly less chloroform administered, and possibly more ammonia, in which the ammonia effect is perfectly clear (242). And here is a similar observation with regard to ether (243). With chlorine water (B.P.) I had precisely similar results; diluted twenty times it was stimulant, undiluted it was promptly depressant.

A more important point, however, with regard to chloroform is the antagonistic effect of $CO_2$. Run $CO_2$ alone through the nerve-chamber for one minute, and after a minute or two of depressed excitability you will witness the usual augmentation. Run chloroform vapour alone through the nerve-chamber, for one minute, and you will witness the usual abolition of excitability, and very probably the abolition may be final. But run the two together by joining up the $CO_2$ apparatus with the $CHCl_3$ bottle, and you will very probably not have to wait long before witnessing a more or less well-marked recovery.

This idea of the stimulant and depressant action of a drug will best be brought clearly to mind by comparing the behaviour with regard to nerve of a group of drugs the action of which has been most abundantly observed upon the human organism, viz., alcohol, chloroform and ether, which together form the now well-known "A.C.E." mixture of anæsthetists. In this case we know already that each of these three reagents are stimulant and depressant, that of A. the salient effect is stimulation, of C. depression, and that in the case of E. the stimulant effect is more marked than in that of C., less marked than in that of A., while the depressant effect of E. is more marked than in that of A., less marked than in that of C.

The evidence of isolated nerve affords precise and elegant confirmation of this result of prolonged experience, and being thus in harmony with such experience signifies that we are in possession of a truthful method. In a series of experiments with different strengths of alcohol, chloroform and ether, respectively, the results come out in a most clear and cogent form, exhibiting as in a nutshell the comparative stimulant and depressant actions of A., of C. and of E.

Here are *e.g.*, the essential data to the point, obtained in a group of five consecutive experiments *ad hoc* upon as many nerves in gas chambers as represented in fig. 2, the reagent being in each case blown in *per* wash-bottle during a period of one minute.

FIVE EXPERIMENTS RE STIMULANT AND DEPRESSANT ACTION OF ALCOHOL, CHLOROFORM AND ETHER.

| | Time. | | Deflection. |
|---|---|---|---|
| 1. | 0— 5 mins. | Undiluted chloroform | 25 mm. (regular). |
| | | | Abolition without preliminary augmentation. |
| | 6—30 ,, | | 0. |
| 2. | 0— 5 mins. | Undiluted ether | 14—13 mm. |
| | | | Abolition without preliminary augmentation. |
| | 6—15 ,, | | |
| | 15—30 ,, | | Trace to 4 mm. |
| 3. | 0— 5 mins. | Undiluted alcohol | 20 mm. (regular). |
| | 5—10 ,, | | 20—25 } *i.e.*, augmentation followed by diminution. |
| | 10—20 ,, | | 21—19 } |
| | 30—40 ,, | | 16—14 } |
| 4. | 0— 5 mins. | Chloroform 1 per cent. | 11 mm. (slightly augmenting). |
| | 5—10—15—20—25—30 mins. | | 11—27—22— 15—8·5—5—3 } *i.e.*, augmentation followed by diminution. |
| 5. | 0—5 mins. | Ether 1 per cent. | 12 to 8 mm. |
| | 5—10—15—20—25—30 mins. | | 8—17—14—11—9—7—5—3 } *i.e.*, augmentation followed by diminution, both less pronounced than in exp. 4. |

And we are justified by such experiments in giving form to our knowledge of the three drugs in this graphic summary, which might also be taken to represent what is admitted to be their action upon the human subject (fig. 10).

Besides these familiar anæsthetics I have (as a preliminary to more systematic examination, and as a further test of the applicability of the method) tried the effects of some of the simpler and less commonly used anæsthetics, such as the chloride, bromide and iodide of ethyl, and several of the various chloromethanes, and chloroethanes that have been tried as anæsthetics.

Here is a memorandum of the anæsthetics whose actions I have compared *inter se* by the method of isolated nerve, with a memorandum of what is probably one of their physical properties by which their physiological effect is most influenced, viz., their boiling-points.[1] I have to

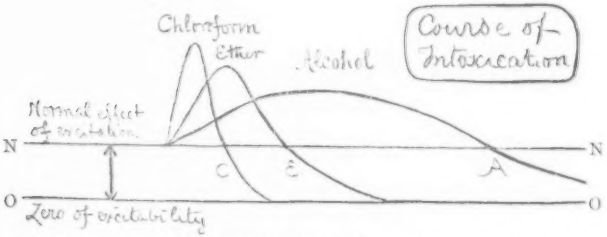


FIG. 10.—Diagram of the excitatory and depressant effects of chloroform, ether and alcohol.

O—O represents the level of zero excitability.

N—N represents the level of normal maximal excitation, and the three curves the stimulant—depressant effects of chloroform, ether and alcohol respectively.

say, however, that I have as yet made no definite tests of this influence, but have only seen in a general way that temperature influences the effect, as indeed do many other circumstances, such as the quality of the nerve, and the reagents to which it may have been previously submitted.

| | | | | |
|---|---|---|---|---|
| $CH_3Cl$ | .. Chloromethane | or Methyl chloride | .. | —23·7°. |
| $CH_2Cl_2$ | .. Dichloromethane | „ Methylene chloride | .. | 41·8°. |
| $CHCl_3$ | .. Trichloromethane | „ Chloroform .. | .. | 61°. |
| $CCl_4$ | .. Tetrachloromethane | „ Carbon tetrachloride | .. | 76·74°. |
| $C_2H_5Cl$ | .. Chloroethane | „ Ethyl chloride.. | .. | 12·5°. |
| $C_2H_5Br$. | .. Bromoethane | „ Ethyl bromide.. | .. | 38·4°. |

[1] $CH\,Cl_3$, $CH\,Cl_2$ should have been omitted from this list as I have not yet obtained it.

| | | | | |
|---|---|---|---|---|
| $C_2H_5I$ .. | Iodoethane .. | or | Ethyl iodide | 72°. |
| $CH_2Cl\,CH_2Cl$ | Dichloroethane | ,, | Ethylene chloride or Dutch liquid .. .. | 83·5°. |
| $CH_3\,CH\,Cl_2$.. | Dichloroethane | ,, | Ethyledene chloride .. | 60·1°. |
| $CH_2Cl.CHCl_2$ | Trichloroethane | ,, | Chloroethylene chloride | 114°. |
| $CH_3\,CCl_3$ .. | Trichloroethane | ,, | Methyl chloroform .. | 76°. |
| $CH_2Cl\,CCl_3$.. | Tetrachloroethane | | .. .. .. .. | 135°. |
| $CHCl_2\,CHCl_2$ | Tetrachloroethane | ,, | Acetylene tetrachloride | 147°. |
| $CHCl_2\,CCl_3$ .. | Pentachloroethane | | .. .. .. .. | 158·9°. |
| $(C_2H_5)_2O$ .. | Diethyl oxide | ,, | Ether .. .. .. | 34·6°. |
| $C_2H_5HO$ .. | .. .. | ,, | Alcohol.. .. .. | 78·5°. |

It is obviously impossible for us to pass all the records of these sixteen reagents through the lantern, nor would such a running review be a very suitable means of forming a conclusion as to their relative efficacy as anæsthetics.

But from the records laid out in order on that side-table, you may, after leisurely inspection, decide for yourselves whether or no the conclusions I am about to draw from them are justified.

First let me ask you to make a distinction between the activity of these reagents with respect to toxicity and their activity in reference to the chief desideratum of an anæsthetic, viz., degree and rate of recovery from profound but not definitive inexcitability. A drug may quickly abolish excitability, but it is toxic rather than anæsthetic if after its removal excitability does not return.

In this respect you will at once pick out the trichlormethane, $CHCl_3$, more familiar to you, perhaps, under the name of chloroform, as of all these drugs in regard to the excitability of isolated nerve, the most *toxic*. You will as unhesitatingly pick out as the apparently most promising *anæsthetic*, the ethyl dioxide $(C_2H_5)_2O$, *i.e.*, ordinary ether or "sulphuric ether." The crowd of records would then to your eye dispose itself in two groups, into the chlorinated group with chloroform at its head, and toxicity as its characteristic action, and the non-chlorinated group with ether at its head, and anæsthesis as its characteristic action. There are indeed two exceptions to this law, the methyl chloride $CH_3Cl$, and the ethyl chloride $C_2H_5Cl$, which, as you see, fall into the ether group, but the exception is

only apparent, for looking to the two ethereal salts $C_2H_5Br$ and $C_2H_5I$, you at once conclude from the similarity between the three that $C_2H_5Cl$ is anæsthetic by virtue of the $C_2H_5$ radicle rather than by the Cl, Br or I appendix —the radicle $C_2H_5$ is the predominant partner. $C_2H_3Br$ and $C_2H_3I$ I have not yet tested, but feel very confident that they would conform to and confirm the law.

Further than this I hardly care to go, although there is much temptation to make further and premature comparison between individual members of the methane and ethane groups and the ethereal halides. But to impress what surely must arouse most serious reflections on a matter very near and practically important from the clinical side, I will pass through the lantern one pair of plates representative of fifteen other similar pairs registered upon fifteen nerves submitted for one minute to the action of ether and of chloroform respectively.

Comment is needless. One is rather inclined to diminish the stress that such documents must produce on the mind by saying: but this is only a frog's nerve, its current of action is a recondite phenomenon, not necessarily co-extensive with physiological action; a nerve fibre is not a nerve cell. But all possible discount made, the fact remains that here in the nutshell of a laboratory experiment lies sharp and concentrated evidence similar in character to the more diffuse, and therefore less pointed evidence of clinical experience.

You will say perhaps, "but your nutshell evidence proves too much; you show that chloroform easily kills nerve, but we know that chloroform only now and then kills a man or woman." Granted—granted also that a naked nerve is a delicate test, that it returns in exaggerated terms its verdict in the ether *v.* chloroform issue. But every anæsthetist—I will not say "chloroformist"—will tell you that a chloroformed patient is hovering between life and death, and that the utmost watchfulness is needed to keep him on this side of a boundary which he sometimes crosses in spite of—or it may sometimes happen—by reason of that watchfulness. Well, the analogy between the clinical event

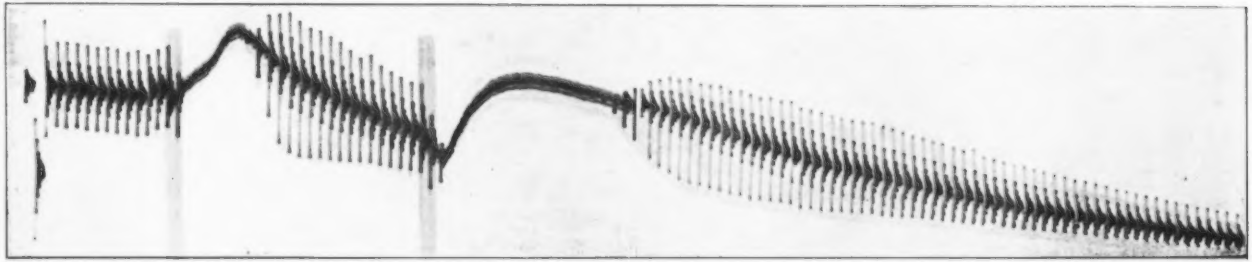


Fig. 11.

Effect of ether, then of chloroform. The latter administered with great care in quantity sufficient to cause temporary and not permanent abolition of excitability.

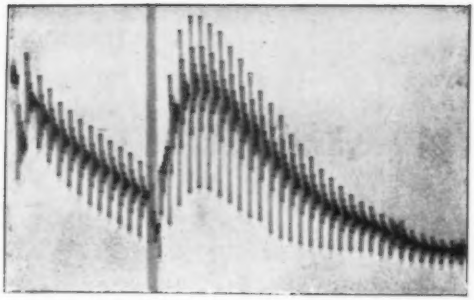

FIG. 12.

Effect of chloroform administered too dilute for anæsthesia, and producing primary excitation passing gradually into a permanent abolition of excitability (from which the subsequent administration of weak ammonia produced only a slight and temporary recovery).

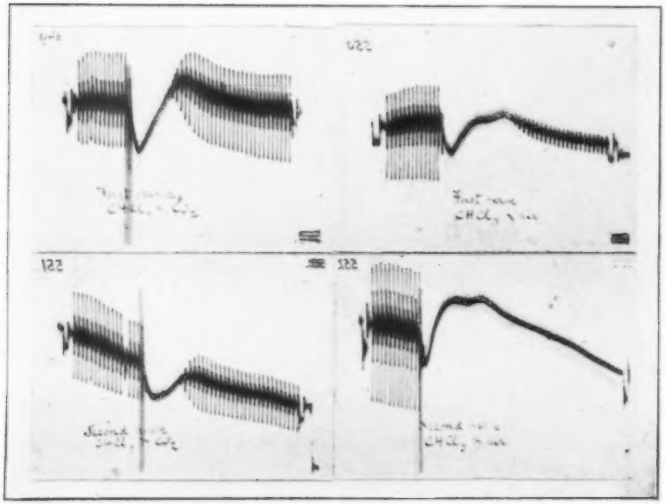


FIG. 13.

A. First nerve, chloroform with $CO_2$.
B. First nerve, chloroform alone.
C. Second nerve, chloroform with $CO_2$
D. Second nerve, chloroform alone

and the laboratory experiments holds even here, only the naked nerve being a finer touchstone than an entire organism irrigated by blood vessels and ventilated by lungs, it is more difficult to *temporarily* anæsthetise by chloroform a nerve than a man. Still it is possible, and I now show you the best instance of successful anæsthesia of nerve I have obtained by carefully graduated chloroformisation (fig. 11). The experiment is a difficult one, and its difficulty illustrates, I think, two opposite dangers of clinical practice—the Scylla "too much" and the Charybdis "too little." You may give your nerve too much, and thus kill it; you may give your nerve too little, and it is, without ever having manifested any sharp suppression of anæsthesia, slowly and steadily drugged to death. Here is such a case: the nerve has been submitted to dilute chloroform vapour, and after manifesting the augmented excitability characteristic of the weak drug, it has steadily died without exhibiting any true anæsthetic state (fig. 12). Thus a nerve—or it may be a patient—can be suddenly struck down and killed by too concentrated chloroform, slowly pressed down and killed by too weak chloroform; just that blow that shall stun without killing is the most difficult to deliver—on nerve at any rate. As far as my experience goes the greater danger—on nerve again—is the "too much" rather than the "too little."

The case of ether has been quite otherwise, using the same delicate test-object of living nerve. I have found it comparatively easy to *temporarily* suppress excitability and to maintain it suppressed during long periods, and it has happened in only one or two instances of "poor" or actually moribund nerves that the suppression has not been succeeded by complete recovery.

As the case stands clinically with respect to ether *versus* chloroform, the question is presented as a *comparison* of two drugs, one more dangerous and more convenient than the other, and an attempt to determine from what quarter danger is most to be expected in the case of the former. That is how the case stands in England; we tabulate death rate statistics, and we appoint commissions

to debate whether chloroform kills by the heart or by the lungs. In American clinics, and in the direct experiments now before you, the comparison is a *contrast* between a safe and an unsafe drug, an anæsthetic and a poison.

It is of course quite beyond my province to discuss in detail the reasons that might on occasion justify the preference of the unsafe drug, more especially as regards the relative gravity of after effects, nor am I disposed to discuss the "safeguards" under which the unsafe drug may be employed for every day purposes, inclusive of minor surgery.

Still, having regard to the fact that on occasion it may be necessary and therefore legitimate to employ the unsafe, but more powerful drug, I will mention two points of detail as the outcome of my nutshell experience.

(1) The idea that chloroform is dangerous according to its impurity, innocuous according to its purity, is erroneous. Pure chloroform free of ethereal impurities is more toxic than impure chloroform containing such. The well-known A.C.E. mixture is less toxic than chloroform alone, more toxic than ether alone.

(2) With regard to the opposed systems of administering chloroform: (*a*) with much diluting air; (*b*) in stronger vapour and exclusive of air; experiments on isolated nerve, *pro tanto*, indicate the second as the less dangerous mode of procedure. $CO_2$ in the nerve-chamber (and *possibly* therefore an excess of $CO_2$ in the lungs and in the blood acting upon the nerve centres) is in its effect an adjuvant of the anæsthetic action and an antagonist of the toxic action of $CHCl_3$ vapour, although it is very evident that obstruction to free aeration, at a time when the blood is charged with chloroform and the organism verging on the limit of "too much," must add to danger, whatever advantage might *theoretically* be hoped for from the primary and secondary effects of $CO_2$ brought into action at the outset of anæsthesia (fig. 13).

Carbonisation during the production of anæsthesia, free aeration during the return from anæsthesia are, as regards isolated nerve, conditions *pro* the anæsthetic, *contra* the toxic effect of $CHCl_3$.

You have, no doubt, learned to carefully remove all obstruction to free aeration during anæsthesia; I cannot venture to advise you to abandon such care: think the matter over, test the point on animals perhaps, before you finally make up your mind how—if chloroform must be used—it may be given with least imprudence.

You may, perhaps, be inclined to say that I have already transgressed the limits of strict experiment, and trespassed by inference upon the domain of clinics. That may be, but I shall defend myself by urging that having once reported experimental results of such obvious practical bearings, I am bound to give the inference as it presents itself to my mind, rather than leave it to be drawn less guardedly and cautiously than seems to me to be desirable. Let me then clearly and explicitly state that I regard these experiments (1) as in high degree confirmatory of the almost universally admitted greater clinical danger of chloroform, and (2) as indicative of a possible good effect of $CO_2$ in the production of chloroform anæsthesia. And as regards this second inference of possibility, let me expressly add that I do not recommend its trial upon the human subject; at this stage it is only indicated as requiring careful trial upon cats and dogs.

## Action of Reagents on Isolated Nerve.

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*(To be continued.)*

# FURTHER OBSERVATIONS ON THE EXCRETION OF URIC ACID IN EPILEPSY AND THE EFFECTS OF DIET AND DRUGS ON THE FITS.

BY ALEXANDER HAIG, M.A. AND M.D.OXON, F.R.C.P.,

*Physician to the Metropolitan Hospital and the Royal Hospital for Children and Women.*

EVER since I published in 1888[1] my first observation on the excretion of uric acid in epilepsy I have been asking myself this question: "Is the uric acid fluctuation a cause or a consequence of the epileptic fit?" And it seems to me that from whatever point of view I look at it, whether I regard the relation of the excretion to the fit, and the fact that the plus excretion of uric acid is the result of a minus excretion which preceded the fit, and could not, therefore, possibly be caused by it: or whether I regard the extensive and important series of parallels between an epileptic fit and a uric acid headache, or when I look at the very powerful effects of uric acid on the circulation, nutrition, and function of many important organs and tissues, I seem to get only one answer from all sides, "Cause."

Now it follows that if uric acid is the cause of the fits we ought to be able by controlling uric acid to control the fits to something like the same extent to which, by controlling the uric acid, we can control the uric acid headache (migraine).

Now my own headaches, and those of quite a large number of fellow-sufferers have been almost absolutely controlled by diet, which controls the uric acid: and the more completely the uric acid is kept out of the blood the more

[1] *Neurologisches Centralblatt*, March, 1888.

completely does the headache remain absent; but the moment that uric acid is introduced into the blood in any quantity the headache begins once more.

Thus my own headaches have fallen from forty to fifty in twelve months down to four or five in the same period, and even these four or five are the results of quite definite introductions of uric acid which could be prevented if greater and more constant care in diet was possible.

I may claim, I think, then, for this headache (migraine) that I have absolutely and completely controlled the attacks both in myself and many others, by clearing the blood of uric acid and keeping it clear.

Can the same be done for epilepsy? My impression is that it will certainly be more difficult to do, but should not be by any means impossible, though the absolute amount of control may be less in the case of the fits than in the case of the headaches.

In headaches there is a large and comparatively slow fluctuation in the excretion of uric acid, *i.e.*, a man has a headache to-day because yesterday in the alkaline tide something interfered with his urate excretion, and he passed out of his body only one half the quantity he usually passes in the same hours; to-day the uric acid held back yesterday adds itself on to the natural excretion, and there is consequently enough in his blood for a few hours to affect blood pressure and the intracranial circulation.

The object I attain by diet is so to reduce the intake and formation of uric acid that the largest quantity he is likely to get in his blood as the result of such a fluctuation, shall never, or only very rarely, be sufficient to affect the blood pressure and the intracranial circulation to a serious extent.

Now in epilepsy (as will appear from my clinical results further on) the fluctuation is shorter and steeper; for two to three hours there is a very powerful retention of uric acid, during which, just as in the corresponding case of headache, the patient feels unusually well and strong; and this is followed in the next two hours by an equally short and sharp plus excretion of all the uric acid held back.

In a word the epileptic wave of excretion runs very high,

but only for a short time, and it is very difficult to keep the general level of uric acid excretion so low that these waves shall not occasionally get high enough to do damage by raising the blood pressure and affecting the intracranial circulation.

I note with much interest in this connection that Dr. Gowers remarks (*Lancet*, 1895, vol. i., p. 1626) that the visual sensations of epilepsy last seconds, those of migraine minutes, while the convulsion of epilepsy lasts minutes, and the paroxysm of migraine hours.

With regard to the parallels between the uric acid headache and the fits of epilepsy, though much has been written on the subject it may not be altogether without interest if I shortly mention the main points here.

Now these two diseases agree in—

(1) Having no morbid anatomy (1).

(2) Being periodical.

(3) Occurring for years or for life.

(4) Occurring together or in alternation.

(5) Being preceded by a minus excretion of uric acid accompanied as usual by feelings of well-being.

(6) Being accompanied by a plus excretion of uric acid, and bearing a generally similar relation to the natural diurnal variations in the excretion of uric acid.

(7) In being worse at or about the menstrual period in women.

(8) In being better during pregnancy and worse after delivery (2).

(9) In being better during fevers and worse after them (3).

In (7), (8), and (9) they both exhibit a remarkable parallel with another disease which is due to uric acid, viz., Raynaud's disease (see "Uric Acid," third edition, p. 353).

(10) In being preceded by high blood pressure (4) and irregular pulse, with coldness and numbness of the extremities and shivering.

(11) In bearing similar relations to gout, rheumatism, and other uric acid diseases.

(12) In being preceded or accompanied by subnormal temperature.

(13) In being followed by a fall of blood pressure and a diuresis (5).

(14) In being similarly related to dyspepsia and gastro-intestinal disturbance however caused.

(15) In being similarly affected by weather and changes of temperature.

(16) In being accompanied by more or less complete suspension of gastro-intestinal digestion and absorption.

(17) In being accompanied or followed by albuminuria (6).

(18) In being preceded by marked changes in or even complete loss of sight (7).

(19) In being similarly related to peripheral neuritis (8).

(20) In being made worse by cold.

(21) In being made worse by administration of quinine, iron (9), or lead.

(22) In being improved by nitrites, acids, or antipyrin (10).

(23) In being relieved by compression of the carotid arteries.

(24) In being more or less completely cured by diet.[1]

With regard to (6) it is remarkable how these two diseases, in common with mental depression, angina, and other similar troubles,[2] tend to attack sufferers in the early morning hours; just as the acid tide of the night is coming to an end, just as the uric acid, which has been for many hours below urea tends with the falling acidity to rise above it, just as the low blood pressure, relaxed arterioles, and quick pulse of the night give place to the high blood pressure,

[1] I give a few references with the above statements in cases where I have not previously given them; but most of the points will be found to be discussed at length in my book, to which I must refer for further information. (1) Wynne, *Lancet*, 1893, vol. ii., p. 434. (2) Oliver, *Lancet*, 1894, vol. i., p. 1295. See also *British Medical Journal*, 1891, vol. ii., pp. 1120 and 1236. (3) *Lancet*, 1894, vol. ii., p. 1438. (4) Féré, *Progrès Medical*, 1889, vol. i., pp. 415 and 434; and vol. ii., p. 26. (5) Féré, *Progrès Medical*, 1888, vol. ii., p. 452. (6) *Archiv de Neurol.*, May, 1892. (7) Gowers, *Lancet*, 1895, vol. i., p. 1626. (8) Charcot, *Progrès Medical*, 1890, vol. ii., p. 83; and Cagney, *Lancet*, 1891, vol. ii., p. 1095. (9) Radcliffe, *Practitioner*, 1883, vol. xxx., p. 95. (10) *Lancet*, 1887, vol. ii., p. 1163.

[2] "Uric Acid," third edition, p. 441, where I quote the interesting observation of Prof. Mays that angina, just like migraine and epilepsy, may be preceded by feelings of well being, which is the proof of a uric acid fluctuation.

contracted arterioles, and slow pulse of the early morning; and these facts have been observed by hundreds of people who did not know that the uric acid fluctuation was the cause of all the other changes, and thus missed the fact that explains them all, and proves that uric acid is the cause of all these diseases.

Here, then, in the early morning hours we have a fluctuation in the excretion of uric acid very similar to that which occurs in the epileptic fit, and it is little wonder that a slight pathological increase of this fluctuation should suffice to produce any or all of the above diseases.

In the third edition of my book I have figures to show all these natural fluctuations in the daily excretion of uric acid, and also those which accompany menstruation in women, and explain the relationship between that function and those diseases; and their relation to pregnancy and fevers admits of similar and simple explanation, but it would lead us too far from our subject to discuss these matters fully here.

With regard to (14) the relation between migraine and dyspepsia is that the dyspepsia precedes the headache and is its cause for dyspepsia, causes a fall of urea, and of the acidity of the urine, and the fall of acidity means that the alkalinity of the blood is increased, and it is immediately flooded by any uric acid available for solution; but if you control the uric acid the dyspepsia will have little or no effect, and further than this it appears, for reasons which will be found in "Uric Acid," third edition, chapter x., that the dyspepsia is itself, to a large extent, due to the presence of excess of uric acid in the body and blood, so that when you have removed uric acid you will have removed both the dyspepsia and the headache which it precipitates. I believe that the connection between these phenomena in relation to the fit of epilepsy is precisely the same as in the case of the uric acid headache.

In all these respects there is the very closest parallel between the uric acid headache and the fits of epilepsy or uræmic, puerperal, and other convulsions.

If both are due to uric acid nothing is more simple than

the causation of this extensive parallelism, but if not it is absolutely inexplicable.

There has recently appeared in the *Archives de Neurologie*,[1] an extremely interesting series of papers by Drs. J. Voisin and R. Petit on Epilepsy as due to Intoxication.

They do not appear to have seen my previous writings and researches, nor have they, as yet, identified or named any poison, so that in this respect I am considerably ahead of them: but their argument for intoxication strongly supports my own, and, moreover, I can show that almost every point on which they lay stress can be absolutely and completely explained if it be granted that uric acid is the toxic substance; and those who have watched my results in these and other directions, will, I hope, have no difficulty in admitting that it is toxic.

I shall now only mention one or two points in their papers that bear on uric acid as the cause of epilepsy.

Thus they lay great stress on the occurrence of gastric troubles before and during the fits, or series of fits: but if the series is coming to an end then the tongue clears and the gastric symptoms subside, but if, on the other hand, the gastric symptoms do not subside, the epileptic phenomena will continue.

The explanation of this is simple enough when we know that every gastric upset brings excess of uric acid into the blood in those who have much of it in their bodies.

The gastric trouble is thus the cause of the uricacidæmia which is the cause of the fits, the malaise, the headache, and all other symptoms, and it (uricacidæmia) in its turn intensifies the gastric upset, and adds putrefaction with possible formation of toxic products.

But the gastric troubles are the result of intoxication by uric acid, even though their result is to increase the toxæmia, for in migraine if you keep the blood clear of uric acid both the gastric troubles and the paroxysm of headache are absent.

With regard to the urine, they point out that there is diminished toxicity before and during and increased toxicity

[1] *Archives de Neurologie*, 1895, Nos. 98, 99, 100, *et seq.*

after the fit, and it is interesting to note the exact parallel between the excretion of uric acid (which the authors have not estimated, though they notice in one case a deposit after a fit) and the toxic substance.

The authors also mention an extremely interesting case, in which a wound that was being dressed stopped bleeding with the onset of a fit, and no pulse could be felt at the wrist: but at the end of the spasmodic stage the pulse reappeared, beating 142, the blood pressure rose, and the wound began to bleed freely once more.

In this case the fit was probably due to stoppage of the heart, which failed before the high blood pressure; and with the fall of blood pressure due to the stoppage of the heart, the circulation practically ceased and the wound stopped bleeding, and the corresponding stasis in the cerebral circulation produced the convulsion; later on, the pressure having fallen, the heart recovered itself and began beating again (see "Uric Acid," third edition, pp. 168 and 210).

Then, after the fit, the pressure rose above normal, though probably not so high as it was just before it, when the heart failed.

I have seen a very large number of cases in which the heart has given obvious signs of impending failure before the high blood pressure produced by uric acid in the uric acid headache (migraine); and these cases differ from the above case of epilepsy merely in the fact that the heart, though threatening to fail, did not fail, and so there was no convulsion. And such severe paroxysms of headache may, just like an epileptic fit, be followed by albuminuria.

Talking of albuminuria reminds me of paroxysmal albuminuria and hæmoglobinuria, which I have long held that this albuminuria resembles ("Uric Acid," third edition, pp. 388 and 391); and so of the blood changes which take place in paroxysmal hæmoglobinuria and anæmia as the result of the presence of an excess of uric acid in the blood stream; and I have therefore been very greatly interested to see that the authors mention that a diminution of hæmoglobin and an increase of hæmatoblasts has been observed in connection with the fits of epilepsy, for this is a change

which I thought might very probably occur in the blood at the time of a fit, because as I have pointed out ("Uric Acid," third edition, p. 366), my own blood varies its quality from day to day, in accordance with the amount of uric acid passing through it.

I had thought of this in the case to be presently related, and Dr. Huntley very kindly examined her blood after one or two fits; but his results were indefinite, and I was unfortunately not able to examine it myself; but I hope to do so in some future cases, as I have yet to learn at what length of time after the fit the blood changes show best: probably after or during the albuminuria, when present.

The authors also point out that the repair of wounds is defective while the epileptic phenomena continue, and only goes on properly after the toxine has been eliminated.

Here, again, we have the work of uric acid, for I have for years been pointing out that opium, which the surgeons use to aid the repair of skin wounds, acts by clearing the blood of uric acid, and thus allowing a free capillary circulation in the skin, which is impossible so long as the blood is full of uric acid; and in the ordinary uric acid headache the signs of defective capillary circulation throughout the body are so obvious that they can hardly be missed, even if there is no "dead hand," or actual Raynaud's disease to draw special attention to them.

Then, again, many troubles of mind and its adjustment, which the authors mention, are so obviously similar in migraine and epilepsy, and after what I have elsewhere shown with regard to them, are so obviously due to uric acid as to need no comment.

As regards causation, the authors point out that epileptics come of a degenerate stock, and one subject to many kindred troubles and defects. I think, however, that much of the degeneration may be a co-result with the epilepsy rather than its cause, and we must not, I think, lose sight of the fact that not a few men whose mental powers have been distinctly above the average have none the less suffered from epilepsy, and that migraine is more common among those that work with their brains, and consequently have fairly good brain power.

As to heredity and predisposition, migraine is intensely hereditary, but the inheritance is possibly, as I have pointed out (BRAIN, Spring and Summer Number, 1893, p. 250), merely anatomical, and concerns simply the size and distribution of the arteries that supply the brain with blood, and the anatomical possibility of a good supply of blood to the brain may account for the greater frequency of migraine among brain workers.

I was much struck with this a few years ago, when a gang of eight man were moving some furniture for me, as I noticed that their foreman was a long way the youngest of the gang: but you had only to look at his face and see that he had more brain, as the saying is, than any three of the others; and it so happened that while working for me he had a typical attack of migraine, and I then found that he was an habitual sufferer, and the only one of the gang who was so.

And there is nothing extraordinary in such an anatomical inheritance, for are not eyes, noses, and teeth similarly inherited with an exactitude which is sometimes marvellous?

But in migraine, if you control the uric acid you may absolutely and entirely neglect the anatomical inheritance, which is an advantage rather than a defect.

Three generations, at least, in my own family have been affected with migraine, but in the second and third generations diet has absolutely and completely controlled it.

Epilepsy, like migraine, may be in part the result of large arteries, and therefore may occur along with considerable mental power (see Sir J. Crichton Browne, *Lancet*, 1895, ii., p. 74, also the same journal, p. 149, where a man who was very intelligent, and suffered from periodical headache and later from epilepsy, was found after death to have a heavy brain), while the eventual crippling and destruction of mind referred to by Sir J. Crichton Browne (prev. ref.) may be a result of the repeated congestion, strain and œdema, produced by the recurring high blood pressure.

It is interesting also to note that the above-mentioned author observed for himself that in "dreamy mental states,"

which he considers to be allied to epilepsy, a diet rich in animal food did harm, and he also quotes cases in which epilepsy was similarly affected by diet.

I quite agree with the authors in their argument that an accumulating poison gives the best explanation of the attacks, and I have been pointing this out for more than seven years, and indicating uric acid as the probable poison.

Then they lay great stress on the liability of women at the menstrual period, and the regularity with which attacks recur at each period: and here, again, uric acid affords a complete explanation, for nothing is simpler than to show that for some days, in every menstrual period, there is a plus excretion of uric acid ("Uric Acid," third edition, p. 188), the greatness of the fluctuation depending on the extent of the functional disturbance in the digestive and other systems, and the amount of uric acid in the body of the patient available for solution.

The same applies word for word to migraine, which bears precisely the same relation to the menstrual periods, and if the uric acid is controlled, the secondary disturbances are diminished or removed.

If the facts I have brought forward regarding the relationship between the fits and the excretion of uric acid stood alone they would be worthy of very careful consideration: but linked as they are to the similar facts about migraine and the further fact of its control and prevention by controlling the uric acid, they amount almost to a demonstration of the causation of epilepsy.

The authors divide epilepsy into (1) Reflex, and (2) Toxic; and the latter is further subdivided into (*a*) that due to Auto-intoxication; (*b*) that due to Hetero-intoxication.

Obviously, uric acid may account for toxic epilepsy of auto-intoxication, but even here a large part of the required uric acid was formed outside the body and introduced with the food, as we shall see presently.

It is, unfortunately, not in my power to study a large number of cases making similar diet alterations in all, hence I have been obliged to study one case with great care; but this plan has also some advantages of its own.

Emma S., age 20, admitted under my care at the Royal Hospital for Children and Women on December 7, 1894.

Her fits began when she was 14 years old. At present they are very regular once a week, and often on the same day each week. Her monthly periods began at 15 years of age, and are said to have been regular (but they have been absent during her stay in hospital). Her father and mother are alive and well, but her mother suffers occasionally from headache. Her eleven brothers and sisters are all in good health.

I examined the urine excreted before, during, and after a large number of her fits, and got uric acid fluctuations identical with those I had found in other cases, or in that first published (previous reference).

She was kept in bed to avoid fluctuations from muscular exertion, or changes of temperature, and then her diet and drugs were altered from time to time with a definite object and according to a pre-arranged plan, for controlling the introduction, formation, and excretion of uric acid.

It will probably suffice if I give the excretions of only one or two fits, as most of them were practically identical, and in all without exception there was a very large excretion of uric acid in the hour following the fit, having a relation of 0 to urea from 1-2 to 1-8.

During the daytime she passed water as far as possible about once every hour, so that when a fit occurred there would be but little admixture of urine in the bladder.

Then if a fit occurred, say at 3 p.m., we had got the urine passed at 2 p.m., and this was called *before*. A catheter was passed at the time of the fit, and what it brought away was called *during*, and then water was drawn or passed exactly one hour after the fit, and that was called *after*.

*After* always contained an excessive amount of uric acid both absolutely and relatively to urea.

*Before* generally contained a normal or subnormal quantity.

*During* sometimes contained a considerable excess, at other times only a slight excess according as the separation corresponded more or less accurately with the changes of secretion; thus, if urine was passed at 4 p.m., and if just as urine was going to be passed at 5 p.m. a fit occurred, then the 5 p.m. urine might be called *during*, but would obviously be mixed with the excretion of say three-quarters of an hour preceding the fit in which the excretion was small.

But bearing these causes of fluctuation in mind one always got

a great excess of uric acid in the hour after the fit, and a more moderate excess in the urine drawn at the time of the fit.

Thus on the day of admission she had a fit.

*Before*, passed at 2.15 p.m., pale straw coloured, 1009, gave—

| | | | |
|---|---|---|---|
| Acidity | = 1·0 cc. of decinormal soda solution. | | |
| Urea | = ·75 per cent. | } 1–23·1 | of uric acid to 23 of urea (nearly). |
| Uric acid | = ·03300 per cent. | | |

*During*, drawn off at the time of the fit at 4.45 p.m., turbid, 1012, gave—

| | | | |
|---|---|---|---|
| Acidity | = 1·2 cc. decinormal soda. | | |
| Urea | = 1·0 per cent. | } | = 1–17 (nearly). |
| Uric acid | = ·06048 per cent. | | |

But, obviously, there was a mixture of *during* with the urine of two and a half hours before the fit.

*After*.—Urine drawn at 5·45 p.m., one hour after the fit, was 60 cc., amber, turbid, 1020, and gave—

| | | | | |
|---|---|---|---|---|
| | | | Per Hour. | |
| Acidity | = 7·6 cc. decinormal soda | = | 4·4 grs. of acidity calculated as oxalic acid. | |
| Urea | 1·1 per cent. | } 1–11 | = 10·1 grs. urea. | |
| Uric acid | = ·10080 per cent. | | = ·92 grs. uric acid. | |

*February* 27, 1895.—Urine of twenty-four hours, ending this morning, was 1275 cc., turbid, 1014, and gave—

| | | | In 24 Hours. | Per Hour. | |
|---|---|---|---|---|---|
| Acidity | 4·0 cc. .. | = | 49·2 grs. | = 2·0 grs. | |
| Urea | 1·8 per cent. | = | 351 grs. | = 14·0 grs. | } 1–38 |
| Uric acid | ·04704 per cent. | = | 9·1 grs. | = ·37 grs. | |

On this day she had a fit, and the urine *during* was lost, the specimen *after* was saved, and was the excretion of exactly one hour.

It was 57 cc., amber, slightly turbid, 1022, and gave—

| | | | | |
|---|---|---|---|---|
| Acidity | 8·4 cc. | = | 4·6 grs. | |
| Urea | 1·8 per cent. | = | 13·8 grs. | } 1–13 |
| Uric acid | ·13140 per cent. | = | 1·03 grs. | |

This shows, as compared with the hourly excretion of the day before the fit, that urea was very slightly diminished after the fit, while uric acid was nearly three times as much after the fit as before it.

We see, then, that the urine, after a fit, has generally these characters: it has a high specific gravity, often very high as compared with before and during. It is often turbid, and deposits urates, or uric acid, or both. It is highly acid—this being, I think, entirely due to the large amount of uric acid (often free uric acid) which it contains, and showing nothing

whatever as to the alkalinity of the blood, which is probably high at the time of such a large excretion of urates.

Take another example, March 10, 1895.

Urine of twenty-four hours, slightly turbid, 1014.

| | | |
|---|---|---|
| Urea | 1·6 per cent. | 1-44 |
| Uric acid | ·03696 per cent. | |

Urine, four hours before fit, 1010.

| | | |
|---|---|---|
| Urea | ·9 per cent. | 1-34 |
| Uric acid | ·02688 per cent. | |

Urine drawn at time of fit, containing, of course, also the excretion of the previous four hours, 1014.

| | | |
|---|---|---|
| Acidity | ·8 cc. | |
| Urea | 1·2 per cent. | 1-40 |
| Uric acid | ·03024 per cent. | |

Urine, one hour after the fit, pale amber, turbid, 1022.

| | | |
|---|---|---|
| Acidity | 5·6 cc. | |
| Urea | 1·0 per cent. | 1-20 |
| Uric acid | ·05040 per cent. | |

Here we have a diminished excretion, 1-44, in the twenty-four hours preceding the fit, a slightly increased excretion, 1-34, in the urine passed four hours before the fit.

A diminished excretion in the urine drawn at the time of the fit, being also the excretion of the four hours preceding it, 1-40, showing that there was a fluctuation in the direction of minus excretion in the hours immediately preceding the fit.

And, lastly, we have a plus excretion in the hour following the fit—this being, I think, probably composed of a very large excretion in the 20-30 minutes following the fit, with a lessened excretion after this, the differences in the suddenness and steepness of the waves of fluctuation accounting for the differences in relation found after different fits.

With regard to the large excretion *after* the fit, we must bear in mind that it is the uric acid in the blood that alters the blood pressure, and affects the intracranial circulation; and it is only after it has been in excess in the blood for some little time, that it begins to be found in excess in the urine.

As regards effects on the blood pressure and intracranial circulation, these are probably most marked just at the time of change from low to high pressure; hence the fit comes early in the uricacidæmia, and precedes the great excretion of uric acid.

See, again, March 19, 1895, urine of twenty-four hours, 1-24.

*Urine at* 9.15 *a.m.*, 1-56.

*Urine at* 12.15 *p.m.*, time of fit, 1·70.

*Urine after fit*, 1.15 *p.m.*, 1·9.

Here we have a rather plus excretion on the day before the fit, a considerable retention before 9 a.m., a greater retention between 9 and 12 followed by a very greatly plus excretion between 12 and 1 p.m.

Evidently the fluctuation which produced this fit began about 7 or 8 a.m., and the retention continued and increased up to about 12 o'clock noon, then followed the opposite and resulting plus excretion, producing the fit at 12.15 and the excretion of 1·9 between that and 1.15 p.m.

The parallel between this fluctuation and that which produces the uric acid headache is almost absolute, the differences are those of time and degree only.

Now we can control the uric acid headache by controlling the uric acid, to an extent which leaves little to be desired; can we control also uric acid epilepsy by the same means?

This was the question I have endeavoured to answer by observing this case, and I chose it in preference to other cases because the history seemed to show that the fits were here remarkably regular in their weekly cycle.

I examined the urine *before*, *during* and *after* more than fifteen of her fits, and the results in all were as regards the main points practically identical with those given, and I would undertake to tell in any case when urine was collected in this manner which was the urine of the hour following the fit. This urine also has a characteristic which I have not mentioned, though it is of very great importance, viz., that when a patient is taking drugs such as an iodide or a salicylate, which give a marked reaction in the urine, such reaction is almost completely absent from the urine passed in the hour following the fit.

I fortunately noticed this point in the urine of the very first case of epilepsy I examined, and I have mentioned it elsewhere[1] as evidence of the very great effects which excess of uric acid in the blood exerts on the circulation of the stomach and intestines, more or less completely suspending digestion and absorption in these viscera; thus explaining also both the oxaluria of paroxysmal hæmoglobinuria[2] and dyspepsia, and the presence of excess of putrefactive products from the intestines in the urine after an epileptic fit. Under these conditions, not only is there no absorption of drugs from the stomach and intestines, but putre-

[1] "Uric Acid," third edition, p. 206.

[2] *Ibid.*, p. 390.

faction soon takes the place of digestion, and the products formed under its influence account completely for the oxalates and excess of æthereal sulphates found later on in the urine.

To suggest, as some have ventured to do, that these putrefactive products found in the urine after a fit may represent the cause of the fit, is to put the cart in front of the horse, make a hopeless muddle of cause and effect, and bring a pea soup fog over a clear sky. The only simple, complete, and efficient explanation is, that the circulatory changes which excess of uric acid in the blood produces, affect, on the one hand, the intracranial circulation and produce the fit, and on the other, the stomach and intestines and bring digestion and absorption to a standstill; failure of absorption explains the absence of the drugs from the urine, and excess of putrefaction explains the production of the products which ultimately appear there. Precisely the same thing also occurs in the uric acid headache, for when this is severe, drugs introduced into the stomach produce absolutely no physiological effect, and do not appear in the urine till the headache is passing off, and if the gastric upset is continued for some time, it often ends in vomiting, and the food is then found to be almost undigested, though it has, perhaps, been in the stomach long enough to have been completely absorbed.

In all these cases if you control the uric acid you will control also the headache, the fits, and the gastric upset—all will improve together, for all are due to one and the same cause, the altered circulation which is common to the whole body.

Now, in the case of Emma S., on December 30, 1894, she had a fit while taking both salicylate of soda and iodide of potassium three times a day, the urine *before* the fit gave lots of iodide when a silver salt was added, and a dark purple with perchloride of iron.

*Urine during* gave distinctly less iodide.

*Urine after* with a relation of uric acid to urea of 1-10, gave no iodide of silver, and only a very slight purple with the iron.

To save space I shall now give the whole of her fits in the form of a table, in which I shall also note the interval between each fit and the one preceding it, health, diet, drugs, and remarks; and we can thus see at a glance any variations presented by the fits and the corresponding variations in diet and drugs made with the object of affecting uric acid.

| No. of Fits. | Date. | Interval. | Health. | Diet. | Drugs. | Remarks. |
|---|---|---|---|---|---|---|
| | 1894. | | | | | |
| 1 | Dec. 7 | 7 days | Average | Ordinary | None | Soon after admission |
| 1 | ,, 19 | 12 ,, | ,, | Milk only | Iodide of mercury, Dec. 10 | 3 in 30 |
| 1 | ,, 30 | 11 ,, | ,, | ,, ,, | 20th, Salicylate of soda, and iod. potssm. | |
| | 1895. | | | | | |
| 1 | Jan. 6 | 7 ,, | Tonsillitis T. normal on 4th | ,, ,, | Salicylate of soda alone | |
| 1 | ,, 18 | 12 ,, | Average | ,, ,, | Salicylate of soda off, 12th | 3 in 32 |
| | ,, 21 | ... | ,, | Milk & fish | None | |
| | ,, 24 | ... | ,, | Milk, fish & meat | ,, | |
| 1 | ,, 31 | 13 ,, | ,, | Milk, fish & meat | ,, | |
| 1 | Feb. 4 | 4 ,, | ,, | Milk, fish & meat | None | |
| 1 | ,, 11 | 7 ,, | ,, | Milk, fish & meat; beef tea added | ,, | 3 in 17 |
| 1 | ,, 17 | 6 ,, | ,, | 16th, beef tea off | ,, | |
| | ,, 21 | ... | ... | Meat off | | |
| | ,, 25 | ... | ... | Fish off | | |
| 1 | ,, 27 | 10 ,, | ,, | Milk only | None | |
| 1 | Mar. 10 | 11 ,, | ,, | ,, ,, | ,, | |
| | ,, 11 | ... | ,, | Milk & beef tea | ,, | 3 in 30 |
| 1 | ,, 19 | 9 ,, | ,, | Milk only; last beef tea on 16th | ,, | |
| | ,, 21 | ... | ... | Tea | | |
| 2 | ,, 25 | 6 ,, | ,, | Farinaceous, with 4 cups tea = 2-3 grs. theine p. dy. | ... | |
| | ,, 29 | ... | T. raised slightly | ... | ... | 3 in 18 |
| 1 | Apl. 2 | 8 ,, | Average | ,, | None | |
| 1 | ,, 6 | 4 ,, | ,, | ,, | ,, | |
| | ,, 11 | ... | ,, | Farinaceous, no tea | ,, | |
| 1 | ,, 17 | 11 ,, | ,, | ,, ,, | None | |
| 1 | ,, 24 | 7 ,, | ,, | ,, ,, | ,, | 3 in 29 [1] |
| 1 | May 5 | 11 ,, | ,, | ,, ,, | ,, | |
| | ,, 6 | ... | ,, | Farinaceous, & tea again | None | |
| 1 | ,, 13 | 8 ,, | ,, | ... | ... | 3 in 26 |
| 1 | ,, 21 | 8 ,, | ,, | ,, | ,, | |
| 1 | ,, 31 | 10 ,, | ,, | ,, | ,, | |

[1] The previous 3 in 18 was probably partly the result of the beef tea.

Her first fit was on December 7, said to be one week after the previous one; her health and diet were those of her ordinary life, and she was taking no drugs.

On December 10 I put her on absolute milk diet, and gave her a mixture containing perchloride of mercury and iodide of potassium.

On December 19 she had a fit, twelve days after the previous one.

On December 20 I stopped the mercury, and gave iodide of potassium and salicylate of soda—leaving the milk diet as before.

On December 30 she had a fit, eleven days after the previous one—making three fits in thirty days.

On January 2, 1895, she got slight tonsillitis, with raised temperature, which became normal on the 4th.

On January 6 she had a fit, seven days after the previous one, but I think that this short interval was probably in part the result of the attack of tonsillitis, which would cause a fluctuation in urate excretion.

After the fit on January 6, the iodide was left off, and the salicylate given alone, and all drugs were left off on January 12.

I now began to test the effects of diet.

On January 18 she had a fit, twelve days after the previous one, while she was still on milk only.

On January 21 fish was added to her diet, and on the 24th meat was added, and she continued to take milk, fish, and meat till February 11, when beef tea was added, and she continued to take milk, fish, meat, and beef tea till February 16, when the beef tea was taken off: on the 21st the meat was taken off, and on the 25th fish was taken off, and she was again on milk alone.

She had a fit on January 31, thirteen days after the previous one, and making three fits in thirty-two days. At the date of the last of these fits she had been on fish for ten days and on meat for seven days.

So far, then, diet had not affected the frequency of the fits, for thirteen days was the longest interval she had had; indeed, it rather seemed as if the addition of flesh food had increased the interval, and I should not be surprised if this was the case, for, in the case of the uric acid headache, taking meat steadily every day does not produce a headache nearly so quickly as taking it only for one day or one meal; and the reason is, that the steady daily introduction of uric acid tends at first to keep the blood clear, while a single dose does not raise the acidity much, and as soon as the acidity falls it gets into the blood, and produces signs of its presence.

The next fit was on February 4, four days after the previous one, and the next on February 11, seven days after that, and the next on February 17, six days later, making three fits in seventeen days—a very different record from the two previous series.

From February 25 to March 11 she was on milk only; on March 11 beef tea was added and continued till March 16.

On February 27 she had a fit, ten days after the previous one, a second on March 10, eleven days after, it being on milk only, and a third on March 19, nine days later, when she had been on milk and beef tea for eight days: this making three fits in thirty days, or the same record as the first two series.

Now came what was rather a surprise to me: on March 16 the beef tea was left off, and on March 21 she was put on farinaceous diet, which includes bread, puddings, and tea, in addition to milk.

She now had a fit on March 25 (or rather two close together, which I count as one, as both were due to the same fluctuation of urates), six days after the previous one; another on April 2, eight days later, and a third on April 6, four days after that, making three fits in eighteen days.

Now, as I say, this was rather a surprise, for though I expected that the beef tea might have some effect, it was left off on March 16, and yet the quickest time of all was the fit on April 6, four days after the previous one.

I confess that at this point I felt rather at sea: but I chanced one afternoon to go into the ward just as she had finished her tea, and looking into her cup I saw that what remained was very dark coloured, and it had evidently been rather strong. This led me to enquire how much tea was included in the farinaceous diet, and I found that she had four breakfast cups a day, two at breakfast and two at tea, and further enquiring as to the amount of tea leaves used to make this amount of tea, and taking it that one pound of tea contains 175 grains of theine, I found that she was thus introducing into her body nearly 3 grains of theine a day.

And as I can show that caffeine, theine, theobromine, and all similar xanthin compounds, are practically equivalent to uric acid, she was thus quietly pouring in the equivalent of at least 20 grs. of uric acid a week.

And it was thus little to be wondered at, that with the help of the beef-tea from March 11 to 16, her fits had been more frequent.

After making this discovery I stopped her tea on April 11, leaving her farinaceous diet otherwise as before.

She now had a fit on April 17, eleven days after the previous one, another on April 24, seven days later, and a third on May 5, eleven days after that, making three fits in twenty-nine days.

On May 6 she was again given tea, her diet being otherwise unaltered, and she had a fit on May 13, eight days after the previous one, a second on May 21, eight days later, and a third on May 31, ten days after that; making three fits in twenty-six days, or slightly quicker than in the previous series.

I now decided that I would try and diminish the frequency of the fits, so I put her on farinaceous diet without tea, and gave her salicylate of sodium with iodide of potassium, the former to eliminate as much as possible of the uric acid she might have in her body, and the second to prevent it from combining with alkali when in the blood: for it is apparently the combination of uric acid with alkali in the blood which produces all the physiological and pathological effects which I have been led to attribute to uric acid. I also allowed her to get up, she having been in bed the whole of the previous period, about six months in all.

With this change of diet and drugs she went without a fit for a whole month, and she had no further attack when she left the hospital at the end of June.

The diet treatment did not cause any loss of weight, as in a case I have elsewhere mentioned,[1] for she kept about 90-91 lbs. during the whole of her stay in the hospital.

And now for a general survey of the fluctuations shown in the table.

The fits, according to history, were very regular—one in a week, or three in twenty-one days. After admission on milk only and some drugs, they fell to three in thirty and three in thirty-two days; then animal food was put on, and they quickened up to three in seventeen days; this was left off again and they fell to three in thirty days; some beef tea and tea were given and they quickened to three in eighteen days; these were left off and they fell to three in twenty-nine days; tea was put on again and they quickened slightly to three in twenty-six days.

And then when tea was left off and some drugs were given

[1] "Uric Acid," third edition, p. 209.

as at first they fell lower than they had been during the whole of her previous stay in the hospital, thirty days elapsing without any fit.

There are no doubt some who would argue that this was all pure chance, and that her fits would have varied in much the same way if no alterations in diet or drugs had been made.

I can only say that such an argument has little in it to recommend itself to my mind; for it almost passes the bounds of possible chance that the fits should by accident have varied in such remarkable correspondence with the changes we made in the uric acid introduction (see "Uric Acid," figs. 23-28 and 43-47).

It leaves out of count also entirely the numerous cases in which a diet free from flesh food has produced a more or less marked alteration in the number of fits,[1] or a diet in which the flesh food is only reduced has produced a distinct reduction.[2]

I have seen it suggested that meat food acts as a general stimulant to the nerve centres, like corn in the food of horses; but in the uric acid headache (migraine) this is certainly not the case, as this headache is not influenced at all by the general level of nitrogenous excretion, but only by the height of uric acid above urea, which is a measure of the quantity of uric acid passing through the blood; and this headache can be produced by the ingestion of uric acid or xanthin compounds equivalent to it, which increase the excretion of uric acid but hardly affect total nitrogen; and in the case narrated in this paper it rather appears as if beef-tea and tea, which introduced xanthin and uric acid, had a similar effect on the fits of epilepsy.

On the other hand, in migraine you may keep urea well above the physiological level (3½ grs. per pound of body weight per day), and provided you do this with milk and vegetable substances which do not introduce much uric acid, there will be no increase of headache.

The point about migraine beyond which there is no appeal

[1] "Uric Acid," third edition, p. 176; *Lancet*, 1895, vol. i., p. 96.

[2] *British Medical Journal*, 1895, vol. i., pp. 1088 and 1420.

is, that if you control uric acid, you control the headache without attending to anything else, and I am now suggesting that the same will be found to hold for epilepsy, only here the control must be more powerful and complete.

It further takes no notice of the fact that it is almost impossible to regard the uric acid fluctuation above described as a consequence of the fits, while it is easy, looking to the important influence which this substance exerts on the nutrition and function of almost all the tissues of the body in the uric acid headache, for instance, to regard it as a cause.

Then I believe that as a matter of fact there are really to be met with all gradations from a mere temporary absence of mind up to a severe epileptic fit, and nothing is more common than slight absence of mind in mental depression, or the uric acid headache (see also Sir J. Crichton Browne, *Lancet*, 1895, vol. ii., p. 4, for many interesting connections between dreamy mental states, migraine, and epilepsy).

In the uric acid headache reasoning is difficult, and has to be forced, and the mind becomes a complete blank for words or for names, which in ordinary conditions one knows almost as well as one's own; on the other hand, either before or after the headache, when the blood is cleared of uric acid, there is mental brightness and well-being, a feeling of pleasure in living and thinking, and work is done at double speed and with comparatively little trouble; and all these things I can answer for it, vary absolutely with the uric acid in the blood.

And not only so, but the nutrition and secretion of every gland in the body, the activity of the muscles, and even the formation of urea, are absolutely controlled and conditioned by the influence of uric acid on the circulation, and this having been proved it is obviously quite within the power of this substance to produce such changes in the cerebral circulation as will amply account for the fits of epilepsy.

I shall not further argue the point, but desire to leave this case to the judgment of the profession; and I have a further object in publishing it, namely, to draw the attention of fellow-workers to the fact that they must give far more

care and attention to the cutting off of all possible introduction of uric acid than they have hitherto done, if they are to succeed in curbing the fits of epilepsy.

It is no use to reduce flesh food to one-half or one-quarter of previous quantities, leaving soup, tea, coffee, cocoa, &c., to be taken as before. Why, these measures would not even prevent the uric acid headache; and epilepsy, as I have shown, is probably a more difficult matter to deal with. Here flesh food must be avoided entirely, and all soups and meat extracts regarded as poisons; while tea, coffee, and cocoa, and all other vegetable substances containing xanthin compounds, are to be regarded as containing uric acid, and used, if at all, only as the merest flavouring.

With such diet alterations I believe that much may be done for many cases of epilepsy: but much care is necessary as it is useless to close one door and leave another open, as I found myself doing in the case of tea; and this may explain my comparatively small success with diet in some previous cases, as I have only recently found out that the above xanthin compounds are equivalent to uric acid.

Meanwhile the facts mentioned above show pretty clearly that the fits of epilepsy and convulsions in general bear an extremely close relationship to the uric acid headache (migraine), and like this are probably functional disorders, due to altered circulation in the brain,[1] such altered circulation again being due to the contracted arterioles, and high blood pressure, which I have shown that uric acid produces.[2] The headache is controlled with almost absolute certainty by a diet which frees the blood from excess of uric acid. I trust we shall yet find that many fits will yield in the same way to well directed treatment.

[1] BRAIN, Spring and Summer Number, 1893, and BRAIN, Spring Number, 1891.

[2] "Uric Acid," third edition, chapter v.

# JAMES BRAID, SURGEON AND HYPNOTIST.

BY DR. J. MILNE BRAMWELL.

James Braid, the subject of this sketch, was born at Ryław House, in Fifeshire, about 1795. He studied at Edinburgh University and, after qualifying as a surgeon, practised for a short time in Scotland; then removed to Manchester, where he remained up to the time of his death.

On November 13, 1841, Braid, for the first time, was present at a mesmeric *séance*, the operator being Lafontaine. At this time mesmeric phenomena were believed to be due either to some mysterious force or fluid, self-deception, or trickery. Braid held the latter theory and, on the first occasion, saw nothing to cause him to alter his views. At the next *séance*, six days later, he noticed that one subject was unable to open his eyes. Braid regarded this as a real phenomenon, and was anxious to discover its physiological cause; and the following evening, when the same case was again operated on, he believed he had done so. After making a series of experiments, chiefly on personal friends and relations, he expressed his conviction that the phenomena he had witnessed were purely subjective, and began almost immediately to place these views before the public, his first lecture being delivered on December 27, 1841.

In 1842 Braid offered a paper on the subject of hypnotism to the Medical Section of the British Association. This was refused; whereupon he gave a Conversazione, at which many members of the Association were present, read his paper, and showed cases. His first work on mesmerism was

entitled "Satanic Agency and Mesmerism reviewed, in a Letter to the Rev. H. McNeile, A.M., of Liverpool, in reply to a Sermon preached by him at St. Jude's Church, Liverpool, on Sunday, April 10, 1842." McNeile had charged Braid with "refusing to state the laws of nature by the uniform action of which mesmeric phenomena were produced." To this Braid replied, that he had always explained the phenomena on physiological and psychological principles, and that McNeile had persistently refused to attend his lectures, or read any account of them.

"Neurypnology, or the Rationale of Nervous Sleep," published by Braid in 1843, and of which 800 copies were sold in a few months, was the first of a series of works on the subject of hypnotism. The necessarily limited length of this article does not permit me to deal with each of these separately and in detail. I propose, therefore, first to give a short account of the theories which appear in "Neurypnology" alone, and then to group together the more important of the facts and views found in the other works.

*Neurypnology.*—At the second *séance* Braid observed that the mesmeric condition was induced by fixed staring, and concluded that the inability to open the eyes arose from paralysis of certain nerve centres and exhaustion of the levator muscles. "I expressed," he said, "my entire conviction that the phenomena of mesmerism were accounted for on the principle of the derangement of the state of the cerebral spinal centres, and of the circulatory, respiratory, and muscular systems, induced by a fixed stare, absolute repose of body, fixed attention and suppressed respiration, concomitant with that fixity of attention. That the whole depended on the physical and psychical condition of the patient arising from the causes referred to, and not at all on the volition or passes of the operator, throwing out magnetic fluid, or exciting to activity some mystical, universal fluid or medium." Braid not only insisted that the condition was a purely subjective one, produced in this mechanical way, but he also claimed to have successfully demonstrated that it could be induced in like manner in persons who had never heard of mesmerism, and who were

ignorant of what was expected of them. In illustration of this, he mentioned that he had hypnotised one of his servants, who knew nothing of mesmerism, by giving him such directions as were calculated to impress his mind with the idea that his fixed attention was required merely for the purpose of watching a chemical experiment with which he was already familiar.

After having established the subjective nature of the phenomena, Braid suggested that these should be called hypnotic instead of mesmeric, and invented the terms hypnotism, hypnotist, hypnotise, &c., which, with little change, still form to-day the recognised terminology of the subject.

Braid induced hypnosis by making the subject look at a bright object, held at such a position above the forehead as was calculated to produce the greatest possible strain upon the eyes and eyelids, while at the same time the mind was to be riveted on the idea of that one object. After hypnotising his patients, he manipulated them in various ways, in order to cause changes in the muscular and circulatory systems; he believed that this excited the different hypnotic phenomena, and played an important part in the cure of disease.

Braid found that he could terminate the hypnotic condition by means of a current of cold air. He also noticed that he could make a rigid limb flexible by blowing on it; that he could restore sight to one eye by the same means, and leave the other insensible; excite one half of the body to action while the other remained rigid and torpid, or make the patient pass from a general state of inactivity of the organs of special sense and tonic muscular rigidity to the opposite condition of extreme mobility and excited sensibility. He acknowledged that he was unable to explain these extraordinary phenomena, but stated that he had no difficulty in reproducing them, that they were independent of any "*rapport*" between operator and patient, and invariably appeared no matter whether the current of air came from the lips, a pair of bellows, the motion of the hand, or any inanimate object.

The subjective explanation of the origin of mesmeric phenomena was not a new one, and had already been given both by the Abbé Faria and Bertrand. Their views, however, if not entirely forgotten, exercised no practical influence on mesmeric theory, and Braid evidently was unacquainted with them when he commenced his mesmeric researches; thus, his conclusions were arrived at independently, and successfully substituted for those universally held in his day. At a later date, when his opponents pointed out the similarity between the theories, Braid asserted that this was more apparent than real, as Faria had attributed everything to the effect of imagination; on this point they differed, but were alike in asserting that neither contact nor magnetic fluid was necessary.

At this time Braid did not believe that the phenomena of hypnotism were the result of attention, for, in speaking of some articles on animal magnetism which had appeared in the *Medical Gazette* in 1833, he said: "In the writer's opinion the phenomena are the result of attention strongly directed to different parts of the body, whereas, by my method the attention is riveted to something outside the body."

In opposition to the theory that hypnotism resembled reverie, Braid said: "Reverie proceeds from an unusual quiescence of the brain, and inability of the mind to direct itself strongly to any one point. There is defect in the attention, which, instead of being fixed on one subject, wanders over a thousand, and even on these is feebly and ineffectively directed. This is the very reverse of what is induced by my plan, because I rivet the attention to one idea, and the eyes to one point, as the primary and imperative condition."

Some experiments Braid made, as to the methods of inducing hypnosis, appear to have first suggested alterations in his hypnotic theory and shaken his faith in the purely physical explanation of hypnotic phenomena. At first he had required his patients to look for a considerable time at some inanimate object until the eyelids closed involuntarily. He frequently found, however, that this was followed by pain and slight conjunctivitis, and in order to avoid this he closed the patient's eyes at a much earlier stage. Despite this he

was able to hypnotise as easily as before and without subsequent unpleasant sensations. This led to further experiment, when he found he could induce hypnosis as readily in the dark or with the eyes bandaged, as in the light and with the eyes uncovered; it being only necessary to keep the eyes fixed and the body and mind at absolute rest. He always failed, however, in young children and in persons of weak intellect, or of restless and excitable minds, who were unable to comply with these simple rules. As he succeeded with the blind, Braid concluded that the impression was made through the mind and not through the optic nerve.

"It is important to remark," he said, "that the oftener patients are hypnotised, from association of ideas and habits, the more susceptible they become; and in this way they are liable to be affected entirely through the imagination. Thus, if they consider or imagine there is something doing, although they do not see it, from which they are to be affected, they will become affected; but on the contrary, the most expert hypnotist in the world may exert all his efforts in vain, if the party does not expect it, and mentally and bodily comply, and thus yield to it."

Braid at first was inclined to believe in phrenology, and thought it possible that the passions, emotions, and intellectual faculties could be excited during hypnosis by simple contact or friction over certain sympathetic points of the head and face. He cited twelve cases in which he believed he had observed these phenomena, and thought that they appeared in subjects who were ignorant of phrenology, and who were not influenced by previous training, or by leading questions and suggestions on the part of the operator. He was not satisfied with these results, however, and stated that it was his intention to conduct a new series of experiments on fresh patients, in order to ascertain to what extent it might be practicable, by arbitrary association, to excite the opposite tendencies from the same point. He also thought it probable that errors might have arisen through the remarkable docility of hypnotic subjects, which made them anxious to comply with every suggestion or indication given by the operator.

*Later Works.*—Braid recognised two distinct hypnotic conditions, which correspond practically with the late Mr. Edmund Gurney's "alert" and "deep" stages. The deep stage was characterised by a condition of torpor more profound than that of natural sleep; the alert by exaltation of the special senses and increase in muscular sense and power, as well as exaltation of certain mental faculties. There were intermediate stages between the two, and frequently one glided imperceptibly into the other. By the sense of smell some persons were able to detect any person known to them, or to find the owner of any glove. They first smelt the glove, and then unhesitatingly presented it to its owner, choosing him from amongst a large company. If the nostrils were stopped, however, the apparent clairvoyant faculty instantly disappeared. The sense of touch and the muscular sense were also sometimes so remarkably increased, as to enable certain subjects to write with great accuracy during hypnosis, when effectual precautions were taken to prevent their being able to see. They crossed the "t's" and dotted the "i's," and could even go back a line, strike out a letter and put it in its proper place. One patient could correct the writing on a whole page of notepaper, but if the relative positions of the paper and table were changed, the alterations ceased to be placed correctly. A full and remarkable account is given of the power possessed by two somnambules of imitating songs, &c., in different languages. One of them was severely tested by several experts, particularly by Jenny Lind, and accompanied her successfully when she sang Swedish and Italian songs, and executed complicated and difficult exercises. This patient was ignorant of the grammar of her own language when awake, and possessed no unusual musical gifts.

Braid found that hypnotism gave him the power of directing or concentrating nervous energy; of exciting the force and frequency of the heart's action and regulating the state of the general and capillary circulation; of influencing the muscular tone and energy, as well as the whole of the secretions and excretions of the body. He could also prevent the pain of operations, and cure a number of

diseases which ordinary treatment had failed to relieve—in fact, excite a variety of phenomena widely different from those occurring in natural sleep, or during the waking condition.

Braid noticed that hypnotised patients, who remembered nothing on awakening, even after having undergone surgical operations, could recall what had passed on being re-hypnotised. He termed this "double consciousness." The operator could also arouse the memory of the hypnotised subject by placing his hand on any part of his body; this was simply a physical aid to the concentration of attention. Braid taught some of his somnambules Greek, Latin, French, and Italian, which they forgot on awaking, but remembered on being re-hypnotised. He was aware of the fact that many hypnotic phenomena could be produced without the subjects having previously passed through a condition in any way resembling sleep. This was described as the electro-biological state—a name which Braid justly termed ridiculous. Despite long perseverance, he never succeeded in hypnotising idiots, and found that one patient who was easily hypnotised in health, became refractory during the delirium of fever. Hypnotism, he thought, explained the prolonged trance of the fakirs and the voluntary suspended animation of Colonel Townsend.

Braid performed a number of minor operations on hypnotised patients without their experiencing any pain; in some of these cases the hypnosis was slight, and there was no interference with the general consciousness or memory. Relief or cure was obtained by hypnotic treatment in the following diseases:—Painful affections of muscles and joints persisting after injury, curvature of the spine, corneal opacity, ophthalmia, heart disease and dropsy, organic paralysis, certain skin diseases, amenorrhœa, leucorrhœa, rheumatism, gout, dyspepsia, constipation, certain forms of deafness, epilepsy, neuralgia, nervous headaches, somnambulism, catalepsy, monomania, idée fixe, delirium tremens, torticollis, and various other forms of muscular spasm, chorea, hysterical paralysis, and aphonia.

In a case of spinal curvature, which had been treated by

ordinary methods for six years without benefit, Braid obtained marked and speedy improvement by removing all mechanical apparatus, and rendering the morbidly weak muscles cataleptic by suggestion. He believed he could cure recent cases in this manner without pain or inconvenience to the patient, and considered mechanical supports —except where there was actual disease of the bone—worse than useless, as they favoured the weakening of the muscles.

In 1845, Braid cited the case of a girl, aged 14, who suffered from various hysterical symptoms and frequent attacks of spontaneous somnambulism and catalepsy; he succeeded in putting himself *en rapport* with her during an attack, and cured her by hypnotic treatment. One day he found her suffering from constipation, and successfully suggested during hypnosis that her bowels should act in five minutes. He mentions this as the first instance he knows of in which action of the bowels was produced by suggestion, and afterwards he was equally successful with other patients.

One of the most remarkable cases was that of a near relative of Braid's, who suffered from rheumatism and from long-standing and extensive opacity of the cornea. Braid hypnotised her for the former affection, when, to his astonishment, the cornea gradually became transparent, and ultimately it required close inspection to detect any opacity.

According to Braid, the hypnotic method was superior to all others for regulating the catamenial functions, and for curing or relieving morbid conditions connected with them. His most brilliant results, however, were obtained in hysterical paralysis, and in many of these all ordinary methods of treatment had entirely failed. He records an interesting case in which he succeeded by suggestion in augmenting and maintaining the secretion of milk. On more than one occasion, Braid succeeded in hypnotising himself, and in obtaining relief from rheumatic pains.

*Theory.*—After referring to the reasons which had induced him to adopt the word hypnotism instead of that of mesmerism, Braid stated that he had come to the conclusion that further alteration in the terminology was necessary.

Under hypnotism had been comprised a series of widely varying stages or conditions, whereas, he thought it ought to be restricted to that state resembling sleep followed on awakening by complete forgetfulness of what had occurred. Of those who were relieved or cured by hypnotism only one in ten reached this stage, and the remainder were apt to imagine they could not be benefited by processes which failed to produce the phenomena the name implied. With the exception of the condition of sleep, just referred to, followed by amnesia, Braid now proposed to substitute the term monoideism for that of hynotism, monoideise for hypnotise, &c., for the following reasons :—No matter in what way the hypnotic state was induced, it was essentially one in which the mind became so completely concentrated upon a single idea or train of thought as, for the time being, to make it dead or indifferent to all other considerations and influences. The various physical phenomena were the result of this mental condition, and were simply exaggerations of what had been observed in the ordinary waking state, when the attention had been fixed on one part or function of the body, and withdrawn from others. The imagination, faith and expectant ideas of the hypnotised subject rendered the influence of attention more powerful than in the ordinary waking condition. The mental and physical phenomena, by whatever processes induced, resulted entirely from dominant ideas in the minds of the subjects. Whether these ideas existed previously, or were induced by the audible suggestions or sensible impressions of the operator, before or after hypnosis, was absolutely immaterial. This theory was first published by Braid in 1847. The fascination of birds by serpents, the phenomena of electro-biology, of table-turning, the gyrations of the odometer of Dr. Mayo, the magnetometer of Mr. Rutter, the movements of the divining rod, the supposed levity of the human body when lifted on the tips of the fingers of four individuals were all, according to Braid, examples of unconscious or involuntary muscular action resulting from dominant ideas. When the attention of man or animal, he said, is absorbed by an idea associated with movement, a current of nervous force is sent into the

muscles and a corresponding motion produced, not only without conscious effort, but even, in many instances, in opposition to the volition. The subject loses the power of neutralising the dominant idea, and is irresistably drawn or spellbound according to the nature of the impression produced and may, in this way, be brought under the control of others by means of audible, visible and tangible suggestions.

In "Neurypnology," Braid stated that he was unable to account for the action of a current of air upon hypnotised subjects; at a later date he gave the following theory. In hypnosis the attention is concentrated upon the particular function called into action, while the others merge into a state of torpor; thus, only one function is active at any one time, and hence intensely so. The arousing of any dormant function is equivalent to superseding the one in action, and he explained, therefore, the termination of a state of muscular rigidity, when a current of cold air was directed to the skin, by suggesting that this called attention to the skin, and withdrew it from the muscular sense.

Braid regarded the following as the chief points of difference between spontaneous and induced somnambulism. Spontaneous somnambulists are impelled to certain trains of action by internal impulses, while the induced tend to remain at absolute rest, and to lapse into a state of profound sleep, unless excited by some impression from without.

Natural and artificial sleep were not regarded by Braid as identical, and the following are further points of contrast in addition to those already mentioned. The pupils are dilated in hypnosis, and the eyelids either quiver continuously, or are firmly closed by spasmodic contractions. In passing into hypnosis, anything held in the hand is grasped still more firmly. There is an increase of the muscular sense, and hypnotic subjects possess an extraordinary power of balancing themselves. Chronic rigidity of the muscles is not followed by corresponding exhaustion. Sometimes, in the hypnotic state, there is excitement, similar to that produced by wine and spirits; at others, there is muscular quiescence, with acute hearing and dreamy, glowing imagination—closely resembling the con-

dition induced by conium. While falling into natural sleep, the mind is diffusive or passive, flitting indifferently from one idea to another, and the subject is unable to fix his attention or to perform any act requiring much effort of will. This state is carried into the sleep, and audible suggestions or sensible impressions, if not intense enough to wake the sleeper, seldom do more than arouse dreams, in which ideas pass through the mind without exciting definite physical acts. On the other hand, the active and concentrated state of mind created by the induction of hypnosis is maintained, and the subject manifests various physical acts in response to direct or indirect suggestion. Another difference is the wonderful power of hypnosis in curing many diseases, which have resisted natural sleep and every known agency for years. For instance, a few hypnotic *séances* of ten minutes each cured a patient who must have had, during his long illness, at least eight years' sleep.

*Magnets, &c.*—In Braid's time, the mesmerists held that magnets, certain metals, crystals, &c., possessed a peculiar power, and, with sensitive subjects, were capable of producing attraction and other remarkable phenomena. Some experienced an unpleasant sensation like an aura; others got headache, attacks of fainting, or catalepsy, with spasms so violent that they apparently endangered life. Frequently there was hyperæsthesia of the special senses, and many saw fiery bundles of light stream from the poles of the magnet. All this was said to happen when the subjects did not see the magnets, and did not know what was being done. Braid performed many experiments in order to test these statements, with the following results:—The phenomena appeared when the patients had preconceived ideas on the subject, or when these were excited by leading questions; but were invariably absent when they were ignorant of what was being done. Pretended magnets also produced the phenomena when the patients knew what was expected to occur. Reichenbach recorded an instance where, by the mere exposure of a sensitive plate in a box with a magnet, an impression had been made, as if it had been exposed to the full influence of light. Braid repeated

the experiment, and also had similar ones performed for him by an expert photographer, and, when all sources of fallacy were guarded against, the results were invariably negative. According to Braid, the mind of the patient alone was sufficient to produce the effects attributed to magnetic or odyllic force, and suggested ideas were capable of exciting a great variety of physical sensations and mental conditions. In 1843, Braid referred to Elliotson's belief in the powers of certain metals, and to Wakley's experiments. The latter, operating with a non-mesmerising metal, made the patient believe he was using a mesmerising one, whereupon she fell asleep; and he concluded that all the subjects were impostors. Braid denied this, asserting that the active agent was simply the imagination, and that the metals were neither mesmeric nor non-mesmeric. In the same way, he explained the action of the wooden tractors which Dr. Haygarth successfully substituted for the metal ones of Mr. Perkins.

As the result of some experiments performed in America, it was stated that certain medicines could manifest their influence through glass. Braid repeated these, and found the result invariably a negative one, when mental influences were excluded. He was able, however, to make a phial filled with coloured water act as an emetic when he confidently predicted this; while a similar phial, placed in the patient's other hand, checked the emetic action when he asserted that it would do so.

By the action of the imagination, Braid explained not only the curative power of homœopathic remedies, but also that of some which had a recognised place in orthodox medicine. Every drug had a two-fold influence; first, that due to its physical properties alone; and secondly, that which resulted from the patient's mental expectation of predicted effects. The influence of the mental attitude of both physician and patient caused remarkable revolutions in the estimate of the powers of particular medicines. At one time a universal favourite apparently possessed every valuable quality; at another, was discarded as utterly worthless, to be again taken into favour at a later date.

*Clairvoyance, &c.*—In Braid's opinion, much of the reluctance to accept the genuine phenomena of mesmerism and hypnotism arose from the extravagant assertions of the mesmerists in reference to clairvoyance—assertions which he described as being opposed to all the known laws of physical science, and a mockery of the human understanding. As the result of frequent experiments made, not only on his own patients, but also upon many of the renowned clairvoyants of the day, Braid was able to find nothing but hypnotic exaggeration of natural powers. The following sources of error, he said, ought always to be kept in mind:—(1) The hyperæsthesia of the organs of special sense, which enables impressions to be perceived through the ordinary media that would pass unrecognised in the waking condition. (2) The docility and sympathy of the subjects, which tend to make them imitate the action of others. (3) The extraordinary revival of memory by which they can recall things long forgotten in the waking state. (4) The remarkable effect of contact in arousing memory. (5) The condition of double consciousness or double personality. (6) The vivid state of the imagination, which instantly invests every suggested idea, or remembrance of past impressions, with the attributes of present realities. (7) The tendency of the human mind, in those with a great love of the marvellous, to erroneously interpret the subject's replies in accordance with their own desires. (8) Deductions rapidly drawn by the subject from unintentional suggestions given by the operator.

Braid considered that the belief in thought transference arose from the failure to guard against sources of error, similar to those just described, and stated that he had never met with any case where the subjects could correctly interpret his unexpressed desires, without some sensible indication of them.

In reference to the alleged intuitive powers of certain mesmeric subjects, Braid stated that, whereas with animals instinct was usually right, with somnambules it was generally wrong. It was true that certain patients could successfully predict their own hysterical attacks, but here

the prophecy produced its own fulfilment through auto-suggestion.

By 1843 Braid had entirely abandoned all belief in phrenology, and stated that the supposed phenomena arose from the touch of the operator calling into action muscles of expression, and thus arousing, by association, certain ideas in the mind of the subject. Sometimes the manifestations resulted from a previous knowledge of phrenology, or from training during hypnosis. In 1844 he showed that he was able to induce all the phenomena by verbal suggestion, no matter what part of the head was touched.

*Suggestions, Passes, &c.*—At first Braid employed mechanical methods alone, both for the induction of hypnosis and its phenomena. But, when he abandoned his physical theory, his views as to the value of passes, &c., naturally changed and he soon regarded them as only of secondary importance, and attached most value to suggestion. With certain impressionable subjects hypnosis might be caused by auto-suggestion; if they believed that something was taking place at a distance, capable of putting them to sleep, they would fall asleep, even if nothing were happening. Direct verbal suggestion, however, was best, both for the production of hypnotic phenomena and for the cure of disease. After hypnotising his patients, Braid stated in a confident manner the results he wished to obtain and, in certain subjects, found that these could be varied by simple change in the voice. Thus, if he made a patient see an imaginary sheep and then asked him, in a cheerful manner what colour it was, this tone usually elicited the reply "white," or some light colour. If he then asked, what colour is it NOW, giving a sad intonation to the word NOW, the reply would usually be "black."

The action of passes, &c., is explained by Braid in the following manner:—Everything which produces a new impression will modify or change existing functions, whether the new impression be of a mental or physical nature. The brain receives many impressions, which subsequently influence the mind, although they were not perceived when conveyed to it by the organs of sense and others, too slight ever

to become conscious, may nevertheless be sufficient to produce a local influence on the nerves and capillaries. Thus, a person may be engaged in reading, so as not to notice he is sitting in a draught, and yet this may cause rheumatism. Passes may have a mechanical action through the agitation of the air or by touch, or they may produce changes in temperature and electrical states. They are most powerful, however, when they directly excite mental action, either by fixing the attention on one part or function of the body and withdrawing it from others, or by arousing ideas previously associated with the physical impression. All these effects may be neutralised by direct suggestion, and it is quite possible, by a system of training, to make passes, &c., produce the opposite of the result usually attributed to them. Thus, "supposing that, with each touch or agitation of the air, the operator speaks aloud and predicts what should happen, the auricular suggestion may be so strong as to cause the predicted manifestation to be realised instead of what otherwise would have been the case; and thus, from this time forward through the double conscious memory, the like impression on that part or organ of sense will recall the previously associated idea of manifestation." Some sort of material combination may be sufficient to produce hypnosis when it is positively affirmed that it will do so, while a moment later the same method will produce nothing, when it is suggested it will be a failure. "All these phenomena may be realised without the patient intending to play off any deception on others, or having any remembrance of the fact on coming out of the sleep."

*Dangers.*—According to Braid, the belief that hypnotism might be used for immoral purposes had arisen through the mesmerists asserting that they could influence patients irresistibly, even at a distance, by mere volition and secret passes. He was certain no one could be involuntarily affected by hypnotism, in any stage of the process, and he could give instructions to even the most susceptible subject by means of which he could completely resist anyone. In his hypnotic experiments he had always observed caution and had neither met with the slightest accident, nor seen a

case which he could not awaken in two minutes. In passing into the hypnotic state, reason and will were the first mental powers to wane; the cerebral spinal functions became more excitable as the controlling powers of the will were withdrawn, and thus the imagination gained the ascendancy. This interference with volition, however, had its limits, and in the alert stage, the patients were even more fastidious as regards propriety of conduct, than in the waking condition; while from the lethargic state, they could be aroused at once to one of exalted sensibility, either by being touched, or by a breath of air; nor was it necessary that this should be done by the person who had hypnotised them. Hypnotism, perhaps, would not make a vicious person virtuous, but certainly it would not make a virtuous one vicious, and there was more chance of extorting secrets by giving the patient a few glasses of wine than by hypnotising him. Braid contrasted the dangers of ether with those of hypnotism, and concluded in favour of the latter, for the following reasons:—All impropriety was strenuously resisted in hypnosis; for example, a patient could not be induced to take off her stockings, or to give a kiss to a gentleman, even should he be a hallucinatory one; on the contrary, she would repel such suggestions with more energy than in the waking condition. Hypnosis quickened the moral sense, while at the same time it rendered the patient docile and obliging in carrying out reasonable suggestions. Thus, while the patient would indignantly refuse to kiss an imaginary gentleman, she would be quite willing to do so to a child. Granting that it were possible to commit a crime during hypnosis, its detection would be inevitable, as the patient when again hypnotised would be certain to remember it; but in ethereal narcotism, there would not be the safeguard of double consciousness, and many powerful medicines had been used for criminal purposes, without the knowledge of the victim. While Braid had never seen any excitement of the animal passions during hypnosis, he had frequently observed spontaneous and intense erotic manifestations arise during the primary stage of etherisation, even in the most modest and virtuous.

*General Observations.*—Braid desired to give full publicity to all his methods and results, and insisted that the phenomena should be examined in the most critical manner, with an honest desire to arrive at truth, as it was impossible to estimate them justly from mere reading or hearsay evidence. He had taken every care to avoid deception, but, as he had been sceptical himself, he did not expect his conclusions would be unhesitatingly accepted.

Braid did not regard hypnotism as a universal remedy, but believed it capable of curing many diseases in which ordinary treatment failed; it was also of use in order to obtain a correct diagnosis. In every case it could be applied with the greatest confidence and absolutely without fear of discomfort, pain or danger. But it was only medical men, well versed in anatomy, physiology and pathology, who were competent to use it with advantage and safety, and the ignorant were warned against tampering with such a powerful agency.

Despite the fact that Braid repudiated the possession of any mysterious force or power, he was more successful than the mesmerists in influencing his patients. He always endeavoured to strip hypnotism of mystery, and believed that he could teach any intelligent medical man how to employ it.

In reference to the almost incredible opposition, both of the orthodox practitioner and the mesmerist, he said: "Like the originator of all new views, however, hypnotism has subjected me to much contention; for the critics, from not perceiving the difference between my method and that of the mesmerists, and the limited extent of my pretentions, were equally hostile to hypnotism as they had been to mesmerism; and the mesmerists thinking their craft was in danger, that their mystical idol was threatened to be shorn of some of its glory by the advent of a new rival, buckled on their armour, and soon proved that the *odium mesmericum* was as inveterate as the *odium theologicum*."

*Historical.*—Braid died suddenly on March 25, 1860, according to some accounts from apoplexy, according to others from heart disease; he left a widow, son and

daughter. He maintained his active interest in hypnotism up to the last, and three days before his death he sent his last MS. to Dr. Azam, with the following inscription: "Presented to M. Azam, as a mark of esteem and regard, by James Braid, Surgeon, Manchester, March 22, 1860."

Sympathetic notices of Braid's death appeared in the local papers and different medical journals, all of which bore warm testimony to his professional skill and high personal character. The *Lancet* drew attention to the fact that, though he was best known in the medical world for his theory and practice of hypnotism, he had also obtained wonderfully successful results by operation in cases of club foot and other deformities, which brought him patients from every part of the kingdom. Up to 1841 he had operated on 262 cases of talipes, 700 cases of strabismus and 23 cases of spinal curvature.

The following are the titles of all the works and articles by Braid which I have been able to trace.

(1) "Satanic Agency and Mesmerism reviewed, in a Letter to the Rev. H. McNeile, A.M., in reply to a Sermon preached by him." (1842, 12mo.)

(2) "Neurypnology, or the Rationale of Nervous Sleep, considered in Relation to Animal Magnetism, illustrated by numerous cases of successful application in the relief and cure of disease." (1843, 12mo, pp. 281.)

(3) "The Power of the Mind over the Body; an Experimental Inquiry into the Nature and Cause of the Phenomena attributed by Baron Reichenbach and others to a 'New Imponderable.'" (1846.)

(4) "Observations on Trance or Human Hybernation." (1850.)

(5) "Electro-Biological Phenomena, considered physiologically and psychologically," from the *Monthly Journal of Medical Science*, for June, 1851, with Appendix.

(6) "Magic, Witchcraft, Animal Magnetism, Hypnotism, and Electro-Biology; being a digest of the latest views of the author on these subjects." Third edition, greatly enlarged, embracing Observations on J. C. Colquhoun's "History of Magnetism." (1852.)

(7) "Hypnotic Therapeutics, illustrated by Cases, with an Appendix on Table-Turning and Spirit-Rapping." Reprinted from the *Monthly Journal of Medical Science*, for July, 1853.

(8) "The Physiology of Fascination, and the Critics Criticised." (1855.) The second part is a reply to the attacks made in the *Zoist*.

(9) "Observations on the Nature and Treatment of Certain Forms of Paralysis." (1855.)

Articles in the *Medical Times*:—

(10) "Animal Magnetism," vol. v., 1841-42, p. 283.

(11) "Animal Magnetism," vol. v., p. 308.

(12) "Neuro-Hypnotism," vol. vi., 1842, p. 230.

(13) "Phreno-Mesmerism," vol. ix., 1843-44, p. 74.

(14) "Mr. Braid on Mesmerism," vol. ix., p. 203.

(15) "Observations on some Mesmeric Phenomena," vol. ix., p. 225.

(16) "Observations on Mesmeric and Hypnotic Phenomena," vol. x., 1844, pp. 31 and 47.

(17) "Case of Natural Somnambulism and Catalepsy, treated by Hypnotism; with remarks on the Phenomena presented during the Spontaneous Somnambulism, as well as that produced by various Artificial Processes," vol. xi., 1844-45, pp. 77, 95, and 134.

(18) "Experimental Inquiry whether Hypnotic and Mesmeric Manifestations can be adduced in Proof of Phrenology," vol. xi., p. 181.

(19) "Magic, Mesmerism, Hypnotism, &c., historically and physiologically considered," vol. xi., pp. 201, 224, 270, 296, 399, and 439.

(20) "Case of Natural Somnambulism, &c.," vol. xii., 1845, p. 117. (Article giving further history of case already reported.)

(21) "The Fakirs of India," vol. xii., p. 437.

(22) "Dr. Elliotson and Mr. Braid," vol. xiii., 1845-46, pp. 99, 120, and 141.

(23) "On the Power of the Mind over the Body; an Experimental Inquiry into the Nature and Cause of the Phenomena, attributed by Baron Reichenbach, and others to a 'New Imponderable,'" vol. xiv., 1846, pp. 214, 252, 273.

(24) "Facts and Observations as to the Relative Value of Mesmeric and Hypnotic Coma and Ethereal Narcotism, for the Mitigation or entire Prevention of Pain during Surgical Operations," vol. xv., 1846-47, p. 381, continued, vol. xvi., 1847, p. 10.

(25) "Observations on the Use of Ether for Preventing Pain during Surgical Operations, and the moral abuse it is capable of being converted to," vol. xvi., p. 130.

(26) "Mr. Braid and Dr. Elliotson," vol. xvii., 1847-48, p. 106.

(27) "Mr. Braid and Mr. Wakley," vol. xvii., p. 163.

(28) "Observations on Trance or Human Hybernation," vol. xxi., 1850, pp. 351, 401, and 416.

In the *Lancet*:—

(29) "Talipes," vol. i., 1841-42, p. 202.

(30) "Queries respecting the Alleged Voluntary Trance of Fakirs in India," vol. ii., 1845, p. 325.

In the *Monthly Journal of Medical Science*:—

(31) "Entire Absence of Vagina, with Rudimentary State of Uterus, and Remarkable Displacement of Rudimentary Ovaries and their Appendages, in a married Female, 74 years of age," vol. xvi. (third series, vol. vii.), 1853, p. 230.

(32) "Hypnotic Therapeutics, illustrated by Cases," vol. viii., third series, 1853, p. 14.

In *Edinburgh Medical and Surgical Journal*:—

(33) "Observations on Talipes, Strabismus, Stammering and Spinal Contortion, and the best Methods of removing them," vol. lvi., 1841, p. 338.

(34) "The Power of the Mind over the Body; an Experimental Inquiry into the Nature and Cause of the Phenomena attributed by Baron Reichenbach and others to a 'New Imponderable,'" vol. lxvi., 1846, p. 286.

(35) "Facts and Observations as to the relative Value of Mesmeric and Hypnotic Coma, and Ethereal Narcotism, for the Mitigation or entire Prevention of Pain during Surgical Operations," vol. lxvii., 1847, p. 588.

(36) "On the Use and Abuse of Anæsthetic Agents, and the best Modes of Rousing Patients who have been too intensely affected by them," vol. lxx., 1848, p. 486.

In the *London Medical Gazette*, new series:—

(37) "Lateral Curvature of the Spine—Strabismus," vol. i., 1840-41, p. 445.

(38) "Stammering," vol. i., p. 445.

(39) "Cure of Stammering," vol. ii., 1840-41, p. 116

(40) "On the Operation for Talipes," vol. ii., p. 186.

Braid is also stated to have contributed a "Case of Cæsarean Section" to one of the medical journals, but this I have been unable to trace.

In 1852, in the Preface to the Third Edition of "Magic, Witchcraft, &c.," Braid stated that he now gave his views in reference to all important hypnotic and mesmeric theories, and hoped, by this means, to make up in some measure for the delay in the publication of another edition of his work on "Hypnotism," which had long been out of print, and was frequently called for. "That call," he said, "I hope shortly to be able to respond to, with such fulness of detail as the importance of its subject merits; more particularly with regard to its practical application for the relief and cure of some forms of disease, of which numerous interesting examples will be adduced." At the conclusion of "The Physiology of Fascination, &c.," he also said: "It is my intention shortly to publish a volume, entitled, 'Psycho-Physiology: embracing Hynotism, Monoideism, and Mesmerism.' This work will comprise, in a connected and condensed form, the results of the whole of my researches in this department of science; and it will, moreover, be illustrated by cases in which hypnotism has been proved particularly efficacious in the relief and cure of disease, with special directions how to regulate the processes so as to adapt them to different cases and circumstances." Shortly before his death, Braid contemplated publishing a second edition of "Neurypnology" in France; this was never done, nor did the two proposed works above referred to, ever see the light. All Braid's books and articles are out of print; and of the former, Nos. 2, 3, 4, 6, and 7 (see list, p. 107-8), are alone to be found in the Library of the British Museum. I possess Nos. 1, 2, 4, 5, 6, and 8; also two long MS. letters addressed to "M. Highfield, Esq., Surgeon," dated re-

spectively October 28, and November 16, 1842. These letters contain an interesting *resumé* of Braid's views on the subjective nature of hypnotic phenomena; some account of the hyperæsthesia of the special senses; reference to successful cases, together with a denial of the alleged dangers of hypnotism, and of the supposed automatism of the subject.

In 1859, Dr. Azam, of Bordeaux, became acquainted with Braid's hypnotic work, and commenced to investigate the subject for himself; an account of his experiments, with much reference to Braid, appeared in the *Archives de Médecine* in 1860. About the same time Broca, who had obtained marvellous results with Braid's methods, read a paper on "Hypnotism" before the Académie des Sciences, which attracted much attention, and Velpeau presented a copy of "Neurypnology" to the same society; whereupon a commission, composed of members of the four sections of the institute, was formed to report on the subject. On hearing of this, Braid wrote to the Académie to say how much pleasure Azam's brilliant results and the action of the society had given him.

From this date, the subject of hypnotism was never lost sight of in France, but it was not until forty years after its original publication that "Neurypnology" was translated by Dr. Jules Simon, who stated that "Braid's researches produced for him numerous enemies, but despite this, he pursued them with the precision of genius, and was able to add artificial somnambulism to the pathology of the nervous system—a chapter which the investigations of the greater number of the modern neuro-pathologists have confirmed."

At the present day, hypnotism is rarely mentioned, either at home or abroad, without due credit being given to Braid for his re-establishment of the subjective explanation of its phenomena. But, apparently, little is known of his later works, and of the remarkable change which took place in his theories. For example, Dr. Bastian, in his article on "Braidism" in Quain's "Dictionary of Medicine," expressed his regret that Braid did not reject all the so-called phenomena of phreno-hypnotism. Professor

Romanes also appears to have been only acquainted with "Neurypnology," and mentions it alone in his article on "Hypnotism" in the *Nineteenth Century* for September, 1880. He refers to the fact that Heidenhain omits all reference to Braid, and maintains that it would be doing scant justice to "Neurypnology" to say that all Heidenhain's results had been anticipated. For, "in the vast number of careful experiments which it ['Neurypnology'] records—all undertaken and prosecuted in a manner strictly scientific—it carried the inquiry into various provinces which have not been entered by Heidenhain. No one can read Braid's work without being impressed by the care and candour with which, amid violent opposition from all quarters, his investigations were pursued; and how, when after the lapse of nearly forty years, his results are beginning to receive the confirmation which they deserve, the physiologists who yield it ought not to forget the credit that is due to the earliest, the most laborious, and the hitherto most extensive investigator of the phenomena of what he calls hypnotism."

The only English writer, as far as I know, who refers to Braid's later works is C. W. Sutton, in the "Dictionary of National Biography," where he states that some of them have been translated into French and German.

The following passage in "Suggestive Therapeutics," published in 1890, shows that, at that date at all events, Bernheim was unacquainted with Braid's advanced theories:—"Braid made use of suggestion without knowing it. We must come down to 1860 to find the doctrine of suggestion entirely freed from all the elements that falsified it, even in the hands of Braid himself, and applied in the simplest manner to therapeutics. The patient is put to sleep by means of suggestion. He is treated by means of suggestion. The subject being hypnotised, Liébeault's method consists in affirming, in a loud voice, the disappearance of his symptoms. Such is the method of therapeutic suggestion, of which M. Liébeault is the founder. He was the first to clearly establish that the cures of pain by the old magnetisers, and even by Braid's hypnotic operations, are not

the work either of a mysterious fluid or of physiological modifications due to special manipulations, but the work of suggestion alone."

The first translator of Braid was W. Preyer, Professor of Physiology at the University of Jena, who, in 1881, published "The Discovery of Hypnotism." This was a condensation of "Neurypnology," together with the translation of the pamphlet sent by Braid to Dr. Azam in 1860, and which had passed into the possession of Dr. Beard, of New York, who had lent it to Preyer. The same pamphlet is also translated into French, and forms an appendix to Dr. Jules Simon's "Neurypnology," published in 1883. It contains an interesting account of many of Braid's later views, and describes in plain and unmistakable language his use of verbal suggestion—a fact which renders almost impossible of comprehension the statements of Professor Bernheim on the subject.

In 1882, Preyer published "Hypnotism," which consisted of a translation of all Braid's works, with the exception of "Neurypnology" and "Satanic Agency."

In the *Zeitschrift für Hypnotismus* for December, 1892, Moll warmly acknowledged Germany's indebtedness to Preyer for his translations, and recognised that the later works were a distinct advance upon "Neurypnology," especially in their psychological explanation of hypnotic phenomena. At the same time, even he apparently failed to grasp how entirely Braid had forestalled the "Suggestion" theory of the Nancy School. He admits, however, that "notwithstanding that many researchers have referred to and valued Braid's writings, the modern works are only in the smallest degree a continuation of his."

The fact that Braid's later theories have been so entirely overlooked is all the more striking, when one realises the firm hold they had taken upon scientific opinion in his day. In illustration of this, it is only necessary to refer to the works of the late Drs. Carpenter and John Hughes Bennett. The former gives a full exposition of Braid's views in his "Principles of Mental Physiology," sixth edition, London, 1881, "Mesmerism, Spiritualism, &c.," and elsewhere. The

following passage from an article in the *Quarterly Review* for September, 1853, shows how thoroughly Dr. Carpenter understood the importance attached by Braid to suggestion: —"The clue to the marvel [mesmerism] was soon found by Mr. Braid, in the concentrated operation of the principle of *suggestion* [the italics are Dr. Carpenter's] . . . and under the guidance of this idea, he has subsequently followed up the investigation with great intelligence, making no mystery of his proceedings, but courting investigation in every possible way." Professor Bennett, in his "Text-book of Physiology," reproduced the explanation of "Braidism," both from the physiological and psychological side, first given by him in 1851. This formed a part of the lecture on hypnotism he gave annually to his students, in which he urged them to investigate a subject destined to revolutionise the theory and practice of medicine.

Above everything, it is worthy of note how Braid at once, by his earlier experiments, exploded the fallacies of the mesmerists, which, till then, had flourished successfully, despite the abusive and absolutely unscientific attacks of the combined medical press. In a later article, I hope to have the opportunity of showing that a thorough acquaintance with Braid's researches would have prevented many errors, both of the school of La Salpêtrière and that of Nancy.

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(2) "Animal Magnetism," vol. v., 1841-42, p. 283. Editorial account of two lectures by Braid, one on March 1, 1842, at Hanover Square, and the other next day at the London Tavern.

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(5) "Hypnotism, or Mr. Braid's Mesmerism," vol. x., 1844, p. 98. Letter to editor from "S." in praise of Braid's researches and of the open-mindedness of the *Medical Times*.

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J. MILNE BRAMWELL.

# Reviews and Abstracts.

*Anatomie des Centres Nerveux.* Par J. Dejerine, Professeur Agrégé à la Faculté de Médecine de Paris, avec la collaboration de Madame Dejerine-Klumpke. Vol. I. Imp. 8vo, 816 pages, with 401 illustrations, 45 of which are coloured. Paris: Rueff et Cie., 106, Boulevard St. Germain, 1895.

This work is the most exhaustive consideration of the subject with which it deals, namely, the anatomy of the cerebrum, which has as yet appeared in any language. It is so complete, both in its facts and in its bibliography, that it ought to be in the hands of every teacher of anatomy and every neurologist.

We propose to limit this notice to an account of the contents of this volume.

The first chapter describes the methods generally employed in the study of the central nervous system. The mode of opening the spinal canal and the cranium, and the removal of the spinal cord and brain are first described, and then an account is given, and deserves careful consideration, of the various modes of section of the brain in the fresh condition which have been recommended by Virchow, Meynert, Pitres, Brissaud and others, and their various advantages and disadvantages are considered. The methods of hardening, embedding and cutting of microscopical sections are described in full detail, the authors using Gudden's microtome for the last purpose.

Fifteen pages are devoted to the various methods of staining, among which we regret to find no mention of Bevan Lewis's process, which, curiously, seems to be little known on the Continent.

The second chapter is concerned with the development of the central nervous axis, and is very fully illustrated with drawings, which are partly original and partly reproduced from His.

The third chapter discusses the development from the histological side, both of the central and peripheral nervous system,

while the fourth chapter discusses the general histology of the central nervous system. Both of these chapters are remarkably full, and include the most important results of the more recent methods.

The second portion of the volume contains the specially original portion of the work of the authors, namely, the anatomy of the cerebrum, and is most minute in its descriptions, and most beautifully illustrated with photographs and original drawings, which have been made in part from macroscopic sections, and in part from microscopic sections stained by the Weigert-Pal method; the accuracy and artistic finish of those drawings we have never seen equalled. A long chapter is devoted to the surface anatomy of the cerebrum, each convolution and its subdivisions, and each fissure being carefully described. The value of the account is greatly enhanced by giving the various synonyms in use by different authors, which are often very confusing. The interior of the cerebrum is illustrated, as already said, by macroscopic and microscopic drawings. Of the former there are sixteen horizontal, thirty vertical transverse, and ten sagittal sections. Of the microscopic sections there are twelve vertical transverse, and twenty-one horizontal, fifteen of which specially illustrate the structure and relations of the basal ganglia. Lastly, there are thirteen oblique longitudinal sections of the subthalamic region. The concluding chapters of the work are concerned with the minute structure of the grey and white matter of the cerebrum, the former of which have been studied specially by the method of Golgi.

We heartily congratulate the authors upon their completion of this monumental work, and trust that it may meet with the success that it merits.

ALEXANDER BRUCE, M.D.

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*Cahier de Feuilles d'Autopsies: Pour l'Étude des Lésions du Névraxe.* Imp. folio, 29 pages, with 25 illustrations. Paris: Rueff et Cie., 106, Boulevard St. Germain, 1895. Par Dr. DÉJÉRINE.

THIS book consists of a series of outline drawings of various aspects of the brain:—vertex, base, outer and inner aspects, horizontal sections at several levels of the cerebrum, vertical

transverse sections of the occipital lobe, Meynert's dissection exposing the upper surface of the corpora striata, the optic thalamus, and the cerebellum, as well as a series of horizontal sections through the corpora quadrigemina, the pons and the spinal cord. The drawings, which are made from nature, are intended to facilitate the description and localisation of lesions of the central nervous system during the course of a *post-mortem* examination, or during the subsequent examination of microscopic sections. A number of valuable hints are given with regard to the manner of making sections in the fresh state, some of which seem to deserve special attention.

Dr. Déjérine recommends the opening of the spinal canal and the removal of the cord before the opening of the cranium and the extraction of the brain. This method allows the cord to be divided transversely between the second and third cervical nerve roots, and thus avoids the loss of tissue produced by the oblique incision made from within the cranial cavity.

Fresh sections should not pass near any lesion, nor any part which is important for the study of secondary degeneration, because the surfaces of the fresh section swell up unequally under the influence of the hardening fluid, and thus a considerable proportion of tissue is lost. In cases of cortical lesion the brain should be hardened without removing the pia mater. The cerebellum should be removed by a transverse incision through the pons, passing below the posterior corpora quadrigeminum, and above the point of emergence of the fifth nerve. The two hemispheres are then separated by an antero-posterior incision, which, in cases of unilateral lesion, should pass at least a centimetre to the sound side of the mesial plane. The hemisphere is then divided into three portions by two vertical, transverse incisions, the anterior of which passes through the knee of the corpus callosum, and just clears the tip of the temporal lobe; while the posterior incision passes through the hinder portion of the splenium of the corpus callosum. The middle portion is further divided into two by a longitudinal incision, which passes at the level of the groove between the caudate nucleus and the optic thalamus. If the lesion is central, it is better to make the original incisions in a longitudinal direction. The upper one should pass through the upper portion of the optic thalamus as just described, and, provided they do not intersect the lesion, additional sections may be made parallel to this at distances of about one centimetre from each other.

In lesions of the cerebellar cortex the basal ganglia of the

cerebrum, crura cerebri, and cerebellum may be hardened together, after being removed from the rest of the cerebrum by Meynert's method. On the other hand, if the cerebellar lesion is central, the lateral lobes of the cerebellum may be removed by two sagittal sections, passing through the flocculus and the middle cerebellar peduncle, external to the point of emergence of the fifth nerve. These directions appear to be of great practical value, especially if the brain be injected with Müller's fluid on three successive days from both carotids and one vertebral artery by Hamilton's method.

ALEXANDER BRUCE.

*Atlas of the Human Brain, and Description of the Course of the Nerve Fibres.* By Dr. E. FLATAU. With Preface by Prof. MENDEL. Translated by WM. NATHAN, M.D., and JOHN H. CARSLAW, M.D. Publisher: F. Bauermeister, Glasgow.

THE object of this work to provide the medical profession with an atlas of photographic illustrations of the normal human brain examined in the fresh condition, unaltered by preserving fluid, and true to nature in details and size, has been most admirably accomplished in the laboratory of Prof. Mendel by Dr. E. Flatau.

There are eight photogravure plates, beautifully executed by Meisenbach, Riffarth and Co., of Berlin, illustrating the various surfaces of the brain and sections through the organ. These include the base with blood vessels; the upper surface; the outer surface; and vertical, horizontal, and sagittal sections. Some of the plates contain two figures, and besides the above most artistic photographic reproductions there are thirteen clear valuable diagrams indicating the course of the afferent and efferent tracts, and the various projection and association systems of the central nervous system.

The illustrations have been chosen with care and discretion, and each figure is clearly numbered, while on the opposite page is a key to the numbers, and no difficulty will be found in distinguishing any of the structures referred to in the plates.

There are twenty-five pages of clear letterpress, translated by Drs. Nathan and Carslaw, which concisely set forth the course

of the fibres in the central nervous system, and embody a brief but clear account of—

(1) The projection fibres of the cerebrum and the cerebellum; and

(2) The association fibres; based upon the latest opinions, as formulated by anatomists and physiologists.

In his preface, Prof. Mendel "hopes that the success of this atlas may be as conspicuous as the industry and care which has been bestowed upon it"; we cordially endorse this statement, and consider that it will be of great use to pathologists and neurologists who are engaged in examining diseased brains.

As it is seldom possible to have at hand for comparison a normal fresh brain in order to determine exactly the localisation of disease, this atlas will be especially valuable to those engaged in making *post-mortems*, particularly in asylums and hospitals for nervous diseases.

F. W. MOTT.

*Les états intellectuels dans La Mélancholie.* Par GEORGES DUMAS, M.D. Paris, 1895.

*La Confusion Mental Primitive.* Par PH. CHASLIN, M.D. Paris, 1895.

*The Insanity of Over-exertion of the Brain.* By J. BATTY TUKE, M.D. Edinburgh, 1894.

THESE three works on insanity, although treating of different forms of disease, are interesting from the fact that the writers approach their respective subjects from three widely differing points of view.

Dr. Georges Dumas' *brochure*, of 140 pages, is principally based on the clinical study of the association of ideas in the simpler forms of melancholia. After analysing cases, in some of which organic conditions, and in others intellectual causes were antecedent; he traces the origin of the melancholic ideas in both to the endeavour of the sufferer to explain, by logical synthesis, the changed emotional state; in other words, to the attempt made by the patient to co-ordinate the ego with the altered affective condition. Thus, if organic conditions are the cause of the

depression, reasons are sought for being depressed. If sad ideas possess the mind, these are justified in the melancholic state, by accessory ideas. So also in aboulia of action or choice; the inability to act or choose is justified or explained, and impulsive action, when beyond all reasonable explanation, is met by the assumption of another ego. The character of Hamlet is ingeniously analysed by the author, at great length, in illustration of these views.

The slowness and painfulness, with consequent limitation and monotony of the mental life, leading to weakness of perception and association, are described, as other modes of the invasion of the ego.

In treating of the relations of the intellectual and organic states in melancholia, he quotes the views of Sollier and Lange, on the connection between the peripheral sensibility and emotion. Sketching the numerous evidences of defective nutrition, and motor activity, &c., in melancholia, and comparing these with similar defects, induced, for example, by paludism (which is often accompanied by mental depression), he concludes that the cœnæsthesia resulting from the bodily state is the actual basis of the melancholy of organic origin.

The melancholy dependent upon ideas of a depressing character arises also, he maintains, by producing similar organic states, the confused perception of which results in emotional depression. The two forms, therefore, are based, he suggests, on the same organic condition; differing only in the order of their development. In support of this view, he quotes Meynert's theory, that physical pain is chiefly made up of motor and vascular reflexes; and argues that psychical pain also, when sudden, as in shock, is followed by mental confusion with movements, accompanied or succeeded by organic depression (fatigue, weakness, hyperthermia, &c.). Melancholia, therefore, whether from organic or intellectual antecedents, is based on the same organic conditions, and is always the consciousness of the state of the body as represented in the cœnæsthesia.

Dumas does not deal with the question why some griefs are not followed (as in his theory they should be) by melancholia, but by mania; nor with such cases as the one Greisinger describes—of a woman melancholic one moment, when her womb was displaced, sane when it was replaced; nor with the fact that the general bodily health may be long depressed, even beyond what is found in marked melancholia, without this result. Neither does he recognise sufficiently that, in paludism and con-

ditions of generally defective nutrition, the nutrition of the brain must be affected with the rest of the body. All these questions have to be answered before M. Dumas' contention can be accepted.

M. Chaslin devotes the first third of his work to the historical literature of mental confusion; three-fourths of this is allotted to French writers on the subject, and, in a brief *résumé*, he concludes that there are two forms—one primary and idiopathic, the other primary and symptomatic.

The idiopathic he describes as developing after a variable, usually short, period of premonitory bodily and mental disturbance, not differing from that preceding the other forms of mental disorder, except by the occurrence of brief attacks of confusion, of which the patient is conscious. The actual onset is sudden or slow, sometimes with exaltation resembling mania, or with agitated melancholia, or with various degrees of stupor, even resembling katatonia.

The appearance of the case is complicated by the combination or succession (with alternations more or less irregular) of the states of exaltation and depression. The essential basis of disorder, however, is mental confusion, with loss of orientation, and with or without delusions, hallucinations, or illusions.

The mean type of the disorder he regards as corresponding to what the Germans call "acute verwirrtheit." The cases differ from melancholiacs in not offering a systematic negation, but in yielding a docile assent to all that they are requested or made to do.

The actions, the facial expression, the speech, the memory, and the perceptions, all show mental obscuration, so that the individual may even have no conception of time, place, or of his own name, age, &c.

Somatic troubles are also very marked, there being general weakness, exhaustion, and defective nutrition; the face pale or flushed, the pupils usually dilated or unequal, trembling of the tongue and muscles of the face, especially in speaking. The pulse small, feeble, and slow; often there is some rise of temperature even to 40° (C.); great emaciation, and the skin dry; the feet and hands often congested. The reflexes variable, movements weak, uncertain, and slow. The urine may contain albumen, sugar, &c., and the menses are arrested. In fact, grave defects of nutrition are always present.

The progress is variable, and the duration months or years; the result—recovery, chronic confusion, dementia, or death.

This description is necessarily, he says, slightly artificial, and so also of the other forms resulting from the different degrees of confusion, of nutritional defect, of excitement, or depression, or from the forms of delusion. If the confusion or intellectual arrest is very marked, the result is acute dementia, restless, or stuporous, if the somatic state predominates, forms result which simulate an infectious disease, and may be called typhoidal or meningitic. Between the two above extremes, a very acute form, of rapid onset, is "*le délire de collapsus*," in which there is a general excitement, extreme confusion, often intense fever, even assuming the aspect of acute mania. Beside this may be placed the "*confusions légères*" of Delasiauve, approximating to neurasthenia, and the more chronic form described by Meynert as amentia. Of these he gives a brief description.

The *primitive symptomatic mental confusion* may be associated with organic disease, or pathological variations of disorder; as examples he quotes cases arising from infectious diseases, especially typhoid, erysipelas, cerebral rheumatism, the acute delirium of infectious origin; the polyneuritic psychosis of Korsakoff; uræmia, diabetes and gout; heart disease, alcoholism, ergotism; meningitis, cerebral tumours, brain syphilis, and some cases of cerebral hæmorrhage; general paralysis, dementia ("precoce" and senile); as well as forms of cerebral softening; folie circulaire, epilepsy, and exophthalmic goitre; while some degree of it results from exposure to extreme cold (Larrey) and from starvation.

In dealing with the pathologic psychology of confusion, he refrains from discussing theories of association, since if synthesis of its elements be admitted as the basis of mental function its loss must be admitted as possible. Confusion, he asserts, is found to be the basis of the mental trouble, independent of hallucinations or delusions, and is constituted by the difficulty and perversion in the association of ideas, &c.

This defect of synthesis affects all degrees of association, from simple perception upwards.

Thus perception of objects is imperfect or perverted, and even where correct the higher reasoning cannot make use of it, or only imperfectly.

The intellectual operations are weakened; the association of ideas and verbal images is defective; imagination is weakened, and reasoning is difficult, or impossible. The memory is generally implicated, the voluntary reproduction of ideas being singularly troubled, as well as their conservation; the power of making new acquisitions does not exist; but automatic reproduction does

occur (even of facts occurring during the illness), but, then, as if unknown to the personality of the patient.

The will is also affected, the acts being difficult, incomplete and awkward; there is loss of the motor images; the synthesis necessary for a voluntary act is defective, and attention (one element of the synthesis) is weakened, words in speech and writing being ill-adapted, phrases and even words being unfinished.

Emotion (the synthesis of innumerable obscure, bodily sensations) is weakened by the disassociation, and is feebly felt; the physiognomy reflecting the mental and emotional uncertainty.

Automatism results from this mental disassociation, and finally abnormal syntheses complicate the condition resulting in the extreme in complete incoherence.

Mental confusion, he asserts, may not only appear primarily, playing the leading part in the disorder, and symptomatically, as before stated, but also secondarily on other psychical conditions.

This secondary confusion may result where the acceleration of ideation is so great that the ideas are transformed immediately into words and acts; or from the mere crowd and whirl of thoughts of which some patients complain; it may arise from numerous hallucinations (especially visual); from sudden emotional change (especially anger and anguish); and lastly, in great variety from intellectual feebleness, congenital or acquired.

He admits that many of these causes of confusion may occur in the same case, *e.g.*, in the "délire de collapsus," and that, consequently, both primary and secondary confusion may be found co-existent.

Primary idiopathic mental confusion, he concludes by defining as an affection, ordinarily acute, following on a cause, usually appreciable (in general an infection), which is characterised by somatic phenomena of denutrition, and by psychic phenomena primarily resulting from the somatic states.

The mental state being constituted by a form of intellectual enfeeblement and disassociation (confusion), which may be accompanied or not by delusions, hallucinations, &c., by agitation or motor inertia, with or without marked emotional variations.

In the chapter on diagnosis, he admits the impossibility of drawing a definite line of demarcation between this and the other forms of disorder; for example, he admits that there may be cases in which it is not possible to say whether the melancholia or the confusion are the predominant factors.

That a state of mental confusion dependent on defective synthesis is the primary and important feature in certain cases of insanity has been fully recognised, and that this defective synthesis while predominant in the cognitive aspect of consciousness, is also marked on the emotional and volitional sides, would also be generally admitted.

M. Chaslin demands the further recognition of this condition as the fundamental factor, in cases in which there are prominent emotional, delusional, or volitional characteristics, and in so doing makes a distinct advance in our views of mental disorder, from a symptomatological outlook, simplifying the arrangement of many cases hitherto ranked under various heads of the voluminous terminology of which a lengthy abstract is appended. Every such generalisation of symptomatology is a probable approach to pathological verity; since the actual abnormal conditions of brain are probably not numerous; the ultimate pathological categories, when arrived at, will certainly bear a minute numerical relation to the symptomatological forms of disorder which burden our text-books.

If confusion be accepted as affecting the basal element (synthesis) of cognition, feeling and volition, it probably denotes a wider disorder of function than attains in states in which only one of these aspects of consciousness is specially involved; and this is confirmed and emphasised by the grave nutritional disturbance accompanying it.

M. Chaslin does not dwell on the prognosis: but as he regards it especially from the side of toxic causation, this, while unfavourable to life in the more acute forms, would be favourable to mental recovery, in proportion to the transient nature of the cause. Yet there can be little doubt that the cerebral condition is more grave than in less complex conditions of disorder.

The writer, in visiting an asylum some years since, was struck by what appeared to him to be the hopeless type of the cases of mania, owing to the presence, in their symptoms, of a great amount of mental confusion; this, however, on inquiry was found to be secondary to the action of a drug which was in vogue at that time, and the prognosis had to be modified in accordance with this fact. Similarly, those cases of melancholia and stupor which manifest much mental confusion are more hopeless than those in which the emotional or volitional arrest is the most striking factor.

The chapter on treatment calls for little comment, being merely a *résumé* of well-known views.

M. Chaslin is undoubtedly to be congratulated on having very carefully collated a very diffuse literature, in a clear and concise form, as well as on the fact of having made a useful generalisation of the confused and conflicting observations on this subject.

"The Insanity of Over-exertion of the Brain," by J. Batty Tuke, is a work of sixty-six pages only, being the Morison Lectures of 1894.

In these lectures Dr. Tuke has applied to his subject the results of recent advances in histological research in the cortical matter of the cerebrum, viz., those made by Ramón y Cajal, Golgi, Lewis, &c., together with the experiments of Hodge, on the effects of expansion on nerve cells.

The first lecture is a summary of the histological structure of the cortex, up to date, accompanied by very satisfactory coloured diagrammatic scheme of its membranes, blood vessels, lymphatics, nerve cells, fibres, &c., the whole being succinctly and clearly described.

In the second chapter, after alluding to Ray and Sherrington's observations, together with those of Langendorf and Geschiedlen, he concludes that the acid products of brain waste may so increase the irritability of the muscular wall of the vessels as to render it more susceptible to vaso-dilator or vaso-constrictor influence.

This lecture is also illustrated by photographs of sections by Hodge, showing very clearly the result of stimulation in the posterior spinal ganglion cell of a cat in four stages, and the morning and evening condition of the sub-œsophageal ganglion of the honey-bee.

He then sketches the course of origin of a subinflammatory condition, from irritation, through active hyperæmia, passive hyperæmia and congestion, together with the results from obstruction of the lympathic system in accordance with the views of the latest histology. In support of this, specimens were exhibited, of which, however, no reproduction is given.

He then briefly summarises the symptoms in cases of insanity from over-exertion of brain function, and concludes that both mania and melancholia are dependent on common pathological conditions, from the fact that during the prodromal period excitement and depression alternate, may co-exist, may pass from one to the other state, even repeatedly as in folie circulaire; also from the similar variations in general paralysis and the sequence of psychical phenomena from poisons such as alcohol.

All this corresponds to the views long since expressed by Dr. Sankey, of the unity of the degenerative processes of insanity.

Dr. Tuke is probably quite right also in attributing the result, in mania or melancholia, in a given case to the intensity and rapidity of incidence of the irritation, in conjunction with the instability of tissue; and in admitting that inherent weakness of the ganglia of the vaso-motor system may have an influence in the rapidity of production of disorder: these also are views to which recent histology add greater probability.

In the third lecture he emphasises the predominant pathologic changes in the Rolandic area, and hazards the opinion that the changes in the convolutions anterior to this region are indicative of impaired nutrition, rather than of active morbid action; "of interruption of trophesial function, which depends on the maintenance of the integrity of cell connection."

He also expresses the conviction that interruption of connection may be brought about by Wallerian degeneration of fibres, processes and collaterals, "the result of structural implication of cells, produced by over-stimulation, and maintained and aggravated by the effects of poisonous exudates."

The general diminution of several functional activities, accompanying such conditions, Dr. Tuke considers is probably due to impairment of the vaso-cerebral system, consequent on nerve implication; while admitting, however, that at present there is no definite proof of this, he quotes the analogy of certain forms of herpes and scleroderma.

He raises a protest against the possible errors in diagnosis and treatment, which may arise from a too facile employment of etiological classification, as exemplified by amenorrhœal insanity, &c.

The abuse of terms, however, it must be remarked, is not sufficient argument for their abandonment.

Dr. Tuke also asserts that for all practical purposes, "peripheral irritation may be dismissed from the list of producers of insanity," a view that does not savour of extensive observation of the early stages of the development of insanity. He also denies that there is sufficient evidence to warrant the connection of insanity with diseases of the heart, liver, or kidneys; although he accepts syphilis as a *vera causa*, he practically dismisses other diatheses.

The lecture on treatment calls for no special remark, except it be an expression of wonder that with the author's views, he is not more emphatic against the use of sedative and narcotic drugs.

In view of the fact that very competent observers have asserted that simple brain work is a rare cause of insanity, it

would have been satisfactory to have had some description of the causation in the cases which the author thus classifies.

In these three works we have mental disorder ascribed, by M. Dumas, to the peripheral cœnæsthesia, by M. Chaslin, to a toxic, hæmic condition, and by Dr. Batty Tuke, to functional overwork. That toxic conditions are sufficiently potent to produce such results there can be no doubt; in theory the first and last might be credited with the possibility of also producing such results. That the first one does do so is, however, extremely doubtful, and the last (overwork) is probably rarely efficient without other associated causes.

Careful studies such as these of the possible modes of action of individual pathological influences are to be highly recommended. They help us on the road to the comprehension of the share in causation of the complex causes almost invariably present in mental disorder, and of the equally complex pathological interactions in which they result.

### Synonyms of Mental Confusion from Chaslin.

Démence aigüe: Esquirol, Brierrè de Boismont.
Stupidité, stupeur: Georget, Ferrus, Delasiauve, Dagonet.
Confusion, confusion hallucinatoire: Delasiauve.
Délire de dépression: Lasègue (?)
Délire d'inanition: Becquet.
Torpeur cérébrale: Ball.
Acute primäre verrücktheit: Westphal.
Hallucinatorischer Wahnsinn: Krafft-Ebing.
Einfache Verwirrtheit: Wille.
Acutes asthenische Delirium: Mayser.
Acuter Wahsinn: Schüle.
Hallucinatorische Verworrenheit: Konrad, Salgo, Scholz.
Asthenische u. hallucin. Verwirrtheit: Kraepelin.
Hallucinatorisches Irresein: Fürstner.
Dementia generalis acuta or subacuta: Tilling.
Mania hallucinatoria: Mendel.
Amentia: Meynert, Serbsky.
Dysnoia, polyneuritic psychose: Korsekoff.
Délire sensoriel: Schereschanski.
Folie générale: Rosenbach.
Paranoïa acuta or hallucinatoria acuta: various authors.
Primary confusional insanity: Spitzka.
Acute hallucinatory confusion: Spitzka.

Stupor, delusional stupor: Hayes, Newington.
Acute confusional insanity: Conolly, Norman.
Frenosi sensoria acuta, confusione mentale, amenza: Morselli.
Stupidità: Morselli.
Delirio sensoriale, Del Greco, de Luzenberger.
Confusion mentale primitive: Chaslin, Séglas, &c.
Paranoïa dissociativa: Th. Ziehen.
Delirium hallucinatorium: Mendel.
Collapsdelirium: Kraepelin, Aschaffenburg (H. Weber).
Erschöpfungsstupor: Schaefer (?).
Acute heilbare Dementia: Binzwanger.
Dementia acuta: several authors.

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*Traité de Chirurgie Cérébrale.* Par A. Broca et P. Mauriac. With 72 figures in the text. Masson et Cie., Paris, 1896.

MM. Broca and Mauriac have written a treatise on cerebral surgery, based upon thirty-one cases which occurred in the hospital practice of M. Broca. The book contains a very complete bibliography, and published facts in cerebral surgery are cited with exactness. The work commences with the anatomy and physiology of the brain, and especially of the convolutions. Considerable space is devoted to the terminology and to the surgical guides for operative measures. From the commencement the authors show a very extensive clinical knowledge; and they devote themselves especially to pointing out in a very clear manner the indications and directions for operation rather than to technical details.

We may also note that the anatomical description is enriched by a number of very valuable, as yet unpublished, descriptions of the convolutions of the brain by the illustrious P. Broca.

In the second part, we find successively the study of traumatic lesions, complications of otitis, tumours, atrophic encephalopathy of infants, hydrocephaly, microcephaly, epilepsy, and encephalocele. Concerning hydrocephaly and microcephaly the authors are especially in favour of operative interference, and M. Broca reports a successful case of drainage of the ventricles for hydrocephaly. Especially valuable is the chapter which deals with the

complications of otitis, and M. Broca, from an extensive experience demonstrates that with practice the most favourable method of dealing with all intracranial complications of otitis is by first opening up the mastoid cells. This book is well got up, and contains seventy-two figures. It should be read by all interested in cerebral surgery.

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*Atlas der Pathologischen Histologie des Nervensystems.* V. LIEFERUNG. *Lésions des cordons posterieurs d'origine exogène.* Mit 10 Tafeln in Heliogravure par G. MARINESCO. Berlin, 1896. A. Hirschwald.

THE author, after considering the origin of the neurons, tries to give a natural classification of the diseases of the spinal cord. He divides the affections of the spinal cord into—

(1) Lesions of the sensory neurons, direct.
(2) Lesions of the sensory neurons, indirect.
(3) Lesions of the motor neurons, direct.
(4) Lesions of the motor neurons, indirect.

These lesions exist either pure or associated. All lesions of the neurons end in sclerosis.

If the lesion commences in *the neuron*, we have "parenchymatous degeneration," terminating in sclerosis. If, however, the lesion is primarily in the *vessels*, we have vascular sclerosis.

Finally, if the degeneration commences in the *interstitial substance*, we have neuroglia sclerosis, *e.g.*, syringomyelia.

The type of direct parenchymatous degeneration of the sensory neuron terminating in sclerosis is tabes.

The authors of this theory, in opposition to the vascular or interstitial theories, believe that parenchymatous degeneration ensues owing to the action of a toxin (syphilitic) upon the ganglion cells of the posterior spinal roots or the collaterals in the spinal cord.

Then follows an explanation of the plates, which represent tabes, cervical tabes, asymmetrical tabes, atrophy of Charcot-Marie, experimental lesion of a single root in animals, and accidental in man.

The author indicates with care the lesions of the collaterals—a hitherto neglected fact. The preparations were made in the laboratory of M. Charcot, at the Salpêtrière.

We can congratulate the author upon this work, which has been executed with great care and exactness. The preparations are faultless, and thus the very beautiful photographic reproductions clearly show all the interesting facts the author so lucidly yet briefly sets forth in the explanatory text. This work is of importance also for the classification the author gives of diseases of the spinal cord, based upon modern views of the structure of the nervous system, and also for those original observations with regard to lesions of collaterals.

This work cannot but be appreciated by all neurologists, and we can cordially recommend it to the readers of BRAIN.

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**Dana on the Localisation of Cutaneous and Muscular Sensations and Memories. (A Study of the Functions of the Motor Area of the Cortex of the Brain.)** *Journal of Nervous and Mental Disease*, December, 1894.

IN an article on "The Cortical Representation of the Cutaneous Sensations" (*Journal of Nervous and Mental Disease*, October, 1888), Dana stated that the clinical and pathological evidence so far collected showed that the motor areas of the cortex contain also the representation of cutaneous sensations; and that the sensory centres for the different parts of the body appear to be larger and more diffuse than the motor. After reviewing the experimental, the clinical and pathological, the anatomical and embryological evidence, and the evidence from teratology, he said:—"I am certain that no amount of scrutiny can explain away the numerous cases in which superficial cortical lesions have caused monoplegias and monoanæsthesias." He believes that the experience since accumulated has confirmed this position. Bastian, in his work on "Paralysis, Hysterical and Functional," has well said, however, that while the sensory function of the so-called motor cortex is acknowledged, the exact nature of this sensory function remains yet to be determined. We have yet to learn the part taken by these areas of the brain in tactile, thermal, muscular, and pain sensations. Dana again goes over this subject, and tries to determine more exactly the sensory functions of this much disputed region. In an article contributed to this subject by Hale White (*Lancet*, September, 1893), the author states that the conditions necessary to furnish perfectly good evidence pathologically of the function of the

central convolutions are very exacting: the lesion must be somewhat limited, it must be definitely localised, its nature must be known by a careful autopsical record, and the clinical phenomena caused by it must have been carefully studied. Very few recorded cases answer all the requirements; still, there are a few that were observed before the first article was written, and there have been some since. There have also been a number of cases in which a certain amount of positive and reliable evidence has been furnished, and careful experimental observations have been made.

*Experimental Evidence.*—Those who wish to study this point are referred to the very complete and thorough article by Mott (*British Medical Journal*, September 23, 1893, p. 685). Mott's experiments were made upon monkeys. He excised certain parts of the motor area; or, rather, he simply cut the cortex from the white matter by introducing a brain-knife bent at an angle. He afterwards tested the amount of paralysis and the defect in sensibility by the clip test, and he found that defective sensibility invariably occurred on the side opposite the lesion.

If the whole leg area were removed, there was paralysis of the opposite leg, permanent as regards the fine movements of the foot, diminished sensibility of the limbs to all forms of stimulus for some days after the operation, and permanent blunting of sensibility to the pressure of a weak clip fixed on the sole of the foot. This was tested on three animals. When the whole motor area was separated, there was permanent paralysis of the hand and foot, and paresis of the other muscles. Such animals showed, for some time after the operation, defective sensibility; only very painful pricking or heat would cause a response, and the parts permanently paralysed were also permanently anæsthetic. Mott infers from his experiments that a permanent defect of tactile sensibility, especially in the hands and soles of the feet, occurs after large lesions of the motor area, something akin to the paræsthesia of ataxia. He found in these cases degeneration of the internal capsule and the striæ medullares of the optic thalamus, with some degeneration of the corpus callosum. There was no degeneration in the posterior longitudinal bundle or the lemniscus, and there was no injury of the gyrus fornicatus.

Schæfer also found that removal of a part of the anterior central convolution produced defect in sensibility as well as motion. He also observed that the area removed must be of a certain size in order to produce this sensibility disturbance; in other words, that the excision of a very small motor area might

produce some motor defect without any detectible sensory defect. Horsley's experiments led to similar conclusions (*Nineteenth Century*, June, 1891).

*Clinical and Pathological Evidence.*

*Case* 1 (personal).—Male, aged 46. History of syphilis ten years before. Patient developed headache, convulsions of the left side of the body, followed by general convulsions and coma. Recovery from the convulsions, with a residuum of complete left hemiplegia and complete hemianæsthesia. Death.

Autopsy showed a syphilitic gumma of the dura mater pressing into and involving the central convolutions. The gumma was located about the middle portion of the fissure of Rolando, and was about one and a half inches in diameter.

*Case* 2 (personal).—Male, aged 55. History of syphilis. Gradual development of right hemiplegia, the paralysis being considerable in extent, and associated with some loss of tactile and pain sensibility on the right side. Death.

*Autopsy.*—Tumour size of hen's egg in middle of left ascending frontal convolution.

*Case* 3 is one of exceptional interest. *Sarcoma, involving hand and arm centre, paralysis, sensory symptoms, Jacksonian epilepsy. Operation. Great improvement.*

Boy, aged 16. At the age of thirteen a blow was received on the head, followed in six months by general epileptic convulsions. Later these became limited to left side, with aura beginning in fingers. A year before operation left arm became gradually weaker, with pains and twitchings in it; intense headache; vomiting and optic neuritis developed. Examination, May 29, 1894, showed paresis of left arm, with very slight paresis of left leg and face; exaggerated reflexes on left side. Sensory condition: Left hand and arm showed diminished sense of contact and pressure; sensory circles enlarged to 2 ctm. (he felt two points as one in this area); localisation of point on hand or arm touched defective; also, defective sense of position; cannot co-ordinate well (partly from paralysis); fumbling and clumsiness; weight sense defective; does not recognise nature of objects placed in hand; temperature sense normal; pain sense slightly exaggerated; no sensory troubles in the leg or face.

Operation by Dr. Conway: Trepanning over middle of anterior central convolution; removal of bone over an area three inches by two and one-half (see fig. 1b). Beneath the dura was found a flat

FIG. 1A.

Case 3. The situation of the trephine opening and of the tumour (from a photograph taken a year after the operation). The dotted line indicates the outline of the trephined area; the dotted area indicates the position of the tumour.

tumour lying on pia, which is attached to it anteriorly; pia mater and cortex infiltrated posteriorly with whitish spots (this area did not react to an electrical current); anteriorly, over the base of the second frontal, the cortex is softened and destroyed by an infiltrating tumour, which is about one-quarter of an inch thick, and extends beyond the limit of the trephine opening. It could not

FIG. 1B.

Case 3. Location and extent of bone removed. At the point where the cross is made (×) the cortex is softened.

be entirely removed anteriorly. Tumour was a spindle-celled sarcoma (Gouley); good recovery was made.

One month later: Pains gone, paralysis improved. Sensory condition practically as before, except that contact sense was improved; no pain; less hyperalgesia; reflex excitability less. Muscular articular sensations slightly more impaired.

Four months later: Paralysis still less; sensory condition about same; no pain; no headaches; *optic nerve normal*; no convulsions. General condition excellent. Patient eloped.

One month later, November 3, 1894, the boy returned, having had several epileptic attacks. He still has no headaches, or eye symptoms. The paralysis and sensory disturbances are about the same.

*Case* 4.—Amelia B., aged 17, single. When six years old had a fall and was struck on the left side of the head. This was followed a week later by a right-sided convulsion. Has since then had convulsions of an epileptic character with loss of consciousness, but always confined to the right side. They increased in frequency to one or two weekly. With them mental deterioration set in, and she became nearly imbecile. Her attacks were unilateral, and began in the right arm, which was raised over the head. Then the head and face and leg were involved. Lately the attacks became general.

*Status presens.*—There was slight weakness on right side, in arm and leg; no anæsthesia or ataxia. The knee-jerks were feeble on both sides, and so were the elbow-jerks.

She was operated upon on September 26, 1894. A piece of bone was removed two inches by one and one-half from over the middle third of the anterior central convolutions, the area extending a little above the middle third and anteriorly over the base of the second frontal convolution (fig. 2).

On removing the bone and opening the dura, both of which were normal, the brain tissue in the anterior part of the wound was seen to be dark and disintegrated. The extent of this could not be exactly ascertained without cutting into the brain unnecessarily. Its superficial area was about one inch in diameter, but might easily have extended down and forwards considerably. A strip one inch long and one-fourth inch wide was removed, and the wound sewed up.

As this case is not reported for its general pathological and clinical interest, further details are not given now.

Three days after operation she had had three right epileptic attacks. Examination at this time showed slight hemiplegia, most marked in lower half right face, less in right arm, least in leg.

*Sensory.*—Tactile anæsthesia was present in the right forefinger, where she could not feel a touch. It was slightly present on the rest of the hand, less still on the face; no anæsthesia of the leg. Analgesia was present in same area as the tactile ænas-

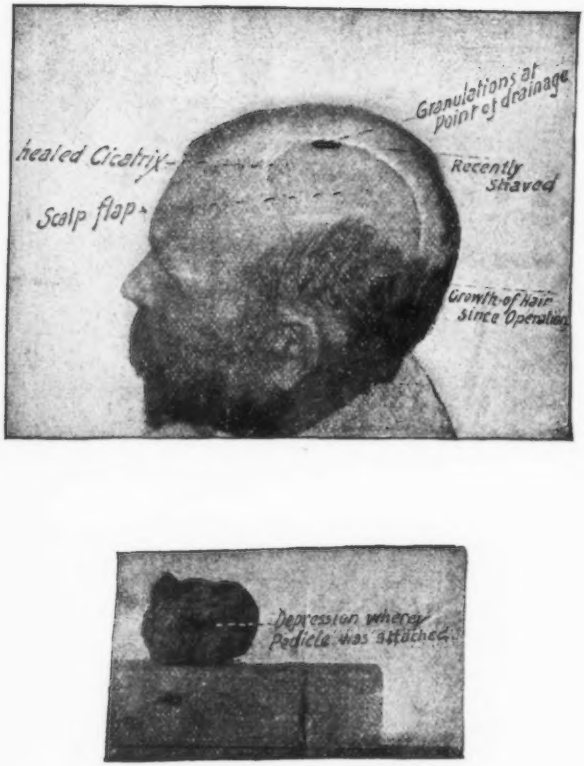



FIG. 3.

Case 5. Showing location and size of tumour in Dr. Steele's case.

thesia. There was no heat or cold anæsthesia. There was great clumsiness and awkwardness in moving the fingers and arm, and a slight difficulty in localising touch. She knew the position of the limbs and fingers.

She could not tell the nature of familiar objects placed in the hand. She could carry the finger to the point of the nose quite accurately.

The striking symptoms were the clumsiness and inability to handle and recognise objects, and the tactile and pain anæsthesia.

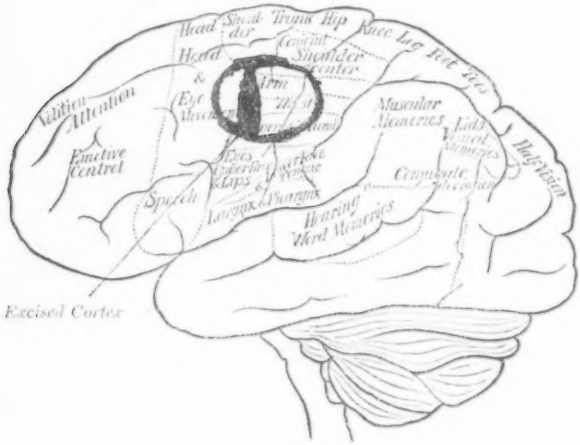



FIG. 2.

Case 4. Showing the area of bone removed and the position of the diseased cortex excised.

Three weeks later slight paralysis remained, the sensory symptoms had disappeared, except a slight awkwardness (more than could be explained by the paralysis). She had had no more convulsions, she seemed brighter mentally and was feeling well.

*Case* 5.—Male, aged 41. Gradual development of pain and paræsthesia in right leg, with Jacksonian epilepsy. At the end of a year the whole right side was affected. Examination then showed right hemiplegia and "sensory blunting" of right side. General symptoms of brain tumour. Operation: A fibro-sarcoma two and one-half inches by two inches was "shelled out" from the region of the upper third of the Rolandic convolutions (fig. 3). The tumour was attached to the falx by a pedicle, and

"grew from the wall of the longitudinal sinus." From this point of origin it grew into the Rolandic fissure, displacing the paracentral lobe. After the operation "sensation was first felt in the shoulder muscles, the next day he could move the arm, and on the third day he could draw up the forearm; and now he has good control of the whole arm except the fingers. He has no power, and but little sensation, in the fingers." He was discharged improved, and improving.—Steele, *Journ. of Amer. Med. Assoc.*, January 27, 1894.

*Case* 6.—This case is reported under the title of a tumour of the cortex, producing hemiplegia, with loss of tactile, pain and muscular sense. A man, aged 51, began to have local epilepsy in October, 1890, the convulsion beginning with paræsthesia, and paralysis marked in left arm. He began to lose tactile, pain and muscular sense in left arm and hand. Loss of tactile sense was absolute in the ring finger. The arm grew weak and the leg began to drag. Gradual increase of paralysis and general symptoms of brain tumour. Death in six months. Autopsy showed a softened melano-sarcoma 1 inch by $1\frac{3}{4}$ inches. "The tumour involved the posterior central, superior parietal, supra-Sylvian anterior portion of angular and occipital convolutions of the right side." The special point is the simultaneous involvement of the arm and hand in paralysis and anæsthesia.—Madden, *Journ. Nerv. and Ment. Dis.*, February, 1893, p. 125.

*Case* 7.—Man, crush of skull just behind right parieto-frontal section, followed by delirium and left hemiplegia. Exploration showed fracture of base as well as vertex. Removal of bone and contused brain over an area four by three inches. No rise of temperature. Return of consciousness on sixth day. Temporary left facial hemiplegia. Paralysis of left arm and leg improved up to a point, so that he could walk well, and left arm showed "good average power." "Voluntary movements were performed with left limbs in extremely awkward manner. He had complete loss of sense of position in the leg, and incomplete in the arm." "He could move the muscles of his face, but could not make a specified movement." Eye muscles normal. "Sense of resistance almost absent." Sense of weight not tested. On the affected side he had sensation of very rudimentary description, these being only tactile (?) and painful sensibility. He could not locate a touch or feel what touched him, but he knew there was contact.

He felt a pinch as painful, but could not locate it. Delayed sense of contact on face, less on arm. He could not distinguish

heat from cold, but if the heat was great it caused a diffuse sense of pain. In the leg the symptoms were similar, but less marked. Other senses normal.

The following parts of the cerebrum would appear to be involved: Lower half of ascending frontal, greater part of sigmoid flexure, posterior third of lower and middle frontal and base of upper frontal. Also, the base of the corresponding part of the falciform lobe. The motor centre for the arm was principally involved (fig. 4).

Electrical tests were made with the galvanic current, one pole on the neck, the other, a small olive-shaped electrode, was placed

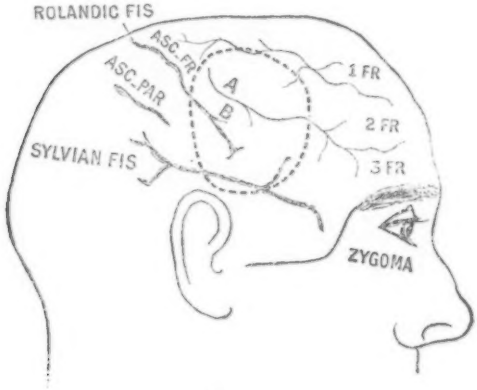



FIG. 4.

Case 7. Laycock. The dotted line shows the extent of the injury to the bone, the letters A and B are placed over the deepest part.

over the face, arm and leg centres. With currents of 5 to 10 ma., paræsthesic sensations were felt over the corresponding segments of the affected side. With stronger currents, 12 to 13 ma., both sides were affected, the right less than the left. There was no pain and no motor reaction. The negative pole gave far more definite results.

Later sensations of burning pain, cramp, and weakness were developed.—Laycock, BRAIN, 1893, vol. xvi., p. 605.

*Case* 8.—C. M., aged 68; tumour of the brain. Focal symptoms were weakness of the left leg, great weakness of the left arm and at the left angle of the mouth; exaggerated knee-jerks.

*Sensory Symptoms.*—There were slightly diminished tactile,

markedly diminished and altered painful, and much diminished thermal sensations all over the left arm and leg and left part of the face and trunk; the sense of position being also very imperfect in the arm and leg, especially the former. No hemiopia and no other affection of any of the special senses. Gradual increase of symptoms, and death about four weeks later.

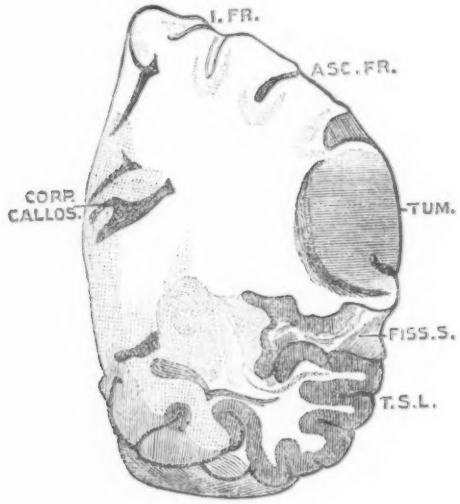



FIG. 5.

Case 8. Scirrhus of brain.

Tracing from a photograph, actual size, of the vertical transverse section passing through the lower end of the right fissure of Rolando. TUM., Tumour. FISS. S., Posterior limb of the fissure of Sylvius. T. S. L., Temporo-sphenoidal lobe. 1 FR., Superior or first frontal convolution. ASC. FR., Ascending frontal convolution. In the temporo-sphenoidal convolutions the grey cortex comes out well, but in the upper part of the section the details are very indistinct, owing to the white softening affecting this part.

*Post-mortem.*—A tumour was found in the right hemisphere, the size of a walnut and hard in consistence, surrounded by a margin of softened brain tissue. It involved the cortex for about an inch and was situated about an inch above the lower end of the fissure of Rolando, entirely replacing the grey matter. The growth was limited to the ascending frontal and parietal convolutions, both of which it invaded at their lower ends (fig. 5). There was white softening of the whole centrum ovale, which it may be assumed was of a date later than that when the examina-

tion that I have described occurred. The tumour was a scirrhous carcinoma. The history of the case showed that the disease began in the face centre. It was accompanied with epileptiform attacks which were associated with a sensory aura.—Wilson, *Lancet*, February 27, 1892, p. 463: "In passing it may be remarked that the occurrence first of a sensory aura (pins and needles) immediately followed by clonic spasm in the same parts, is of interest in connection with the theory that the motor area of the cortex contains sensory cells."

*Case* 9.—Male, 39. For two years Jacksonian epilepsy involving right leg chiefly, but with pain and spasm in right hand. Later, "constant and excruciating pain" in right hand and fingers, slight weakness of right side, right arm in rigid flexion, "tactile sensation fairly acute," skull opened over middle of left central gyrus and posterior part of third frontal. Small tumour lay on cortex. Cortex decorticated one-fourth inch deep over area larger than a dollar in the anterior two-thirds of opening. Next day right hemiplegia most in hand, no more pain in hand. "Sensation fairly acute." Can't speak. On seventh day, less paralysis. "With closed eyes cannot locate a pin prick on right side, but feels it promptly and keenly." Later, relapse. Some return of pain and convulsions. Paralysis improved.—Frank and Church, *Amer. Journ. Med. Sciences*, July, 1890.

*Case* 10.—A patient with Jacksonian epilepsy and symptoms indicating cortical tumour. Operation; no tumour found. Resection of cortex for space 1½ by 1 ctm. No fever. Patient developed a complete hemiplegia, which disappeared at the end of a month, "leaving only a slight anæsthesia and ataxia of the fingers, which prevented him from pursuing his occupation as a tailor."—Dunin, *Verhandl. des X. Intern. Med. Congress*, Band iv., p. 11.

*Case* 11.—Male; cortical degeneration, result of an injury. Before operation, sensibility normal. During operation of trephining cortex of left ascending parietal on level with first frontal gyrus was somewhat lacerated. A small bit of cortex, 3 by 6 mm. and 2 mm. thick, was excised. Entire injured surface had a diameter of not over 1½ ctm. For at least seven weeks after operation patient had "anæsthesia of right arm up to elbow, for touch, pressure, motion and position, sensibility to pain, heat and cold was retained." There was also impairment of highly purposive movements, inco-ordination and a little athetosis.—P. C. Knapp, "Intra-Cranial Growths," p. 61.

*Case* 12.—Man, aged 44. Received a blow on the left side of the head, causing a comminuted fracture. It was followed by a paralysis of the right shoulder and arm, with pain. Operation with removal of bone and contused brain tissue (fig. 6).

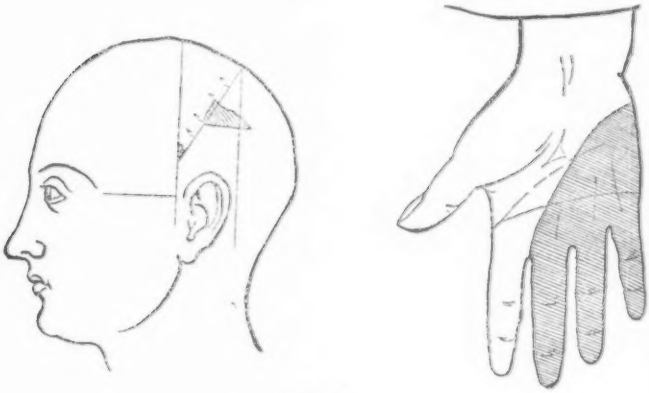


FIG. 6.

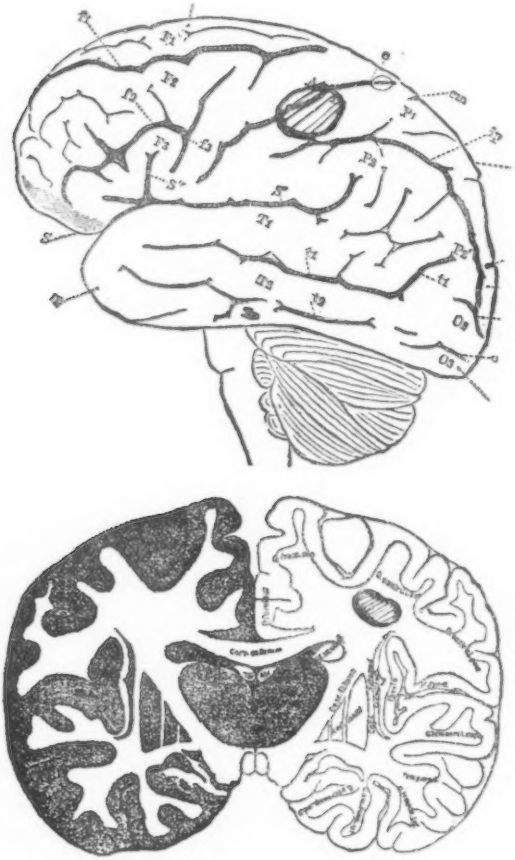
Case 12. Dr. J. Lynn Thomas. Showing location of scar with reference to fissure of Rolando, and the area affected with local hyperidrosis.

The wound healed and paralysis gradually improved. Later it progressed again, and six months after the wound the situation was as follows:—Weakness of left arm and hand; paralysis of the interossei and abductor of the little finger. Diminution of tactile sensibility in the upper third of the forearm. Two years later he could flex the fingers and use the hand to write. Tactile sensibility was lessened in the forearm and hand; sensibility to pain lessened in same region. Thermic sensibility slightly increased. Some hyperidrosis of the right hand.—J. Lynn Thomas, *Brit. Med. Journ.*, February 24, 1894, p. 400.

*Case* 13.—Male, aged 34, gradual development of right brachial monoplegia with symptoms of brain tumour. The lower extremity and face were not at all involved. Patient had phthisis. There was "a very marked diminution of sensibility of all forms, in the periphery more than in the parts near the trunk." No disturbance of sensibility, except in the arm.

*Post-mortem* showed a tubercular tumour in the white matter just below the arm area of the cerebral convolutions. Its exact

position is shown in the accompanying figures, taken from the original (figs. 7, 8).—L. Darkschewitz, *Neur. Centralbl.*, vol. ix., 1890, No. 23.



FIGS. 7, 8.

Case 13. Showing location of tubercular tumour in Darkschewitz's case.

*Case* 14.—Male, aged 40. Traumatic hæmorrhage of pia mater, compression of Broca's convolution and of middle central convolutions, aphasia, partial right hemiplegia and hemianæs-

thesia. Trephining. Clot found and removed. Arm totally paralysed; tactile and pain senses impaired on paralysed side. Three years after operation paralysis of right hand remains, "with marked diminution of tactile and pain sense. . . . The muscular and temperature senses are perfect" (fig. 9).—Starr, "Brain Surgery," Case 18, p. 161.

*Case* 15.—Boy, aged 12. Right hemiplegia with athetosis, due to fall at age of 2. Trephining and cavity in middle of anterior cerebral convolution incised and drained. After operation, hemiplegia the same; "the right hand as high as the

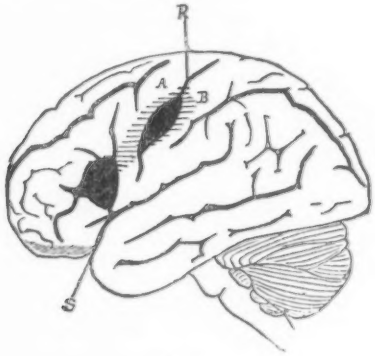



FIG. 9.

Case 14. Starr. Diagram of the left hemisphere of the brain, showing the situation of the clot.

wrist was decidedly anæsthetic to touch, temperature and pain, but there was no affection of the muscular sense" (fig. 10). One week later anæsthesia much less, athetosis gone.—M. A. Starr, "Brain Surgery," p. 38, Case 5.

*Case* 16.—Boy, aged 15. Blow on head, followed in twenty-four hours by paresis of right arm and leg, but not of face or arms. "The grasp of the right hand was less than half that of the left. The pain sense, while not destroyed, was greatly inhibited. The temperature sense was somewhat interfered with. His arm could be moved, but none of the delicate movements of fingers, hand, or forearm could be made. He could not tell the difference by touch between my silk handkerchief and the woollen blanket on his bed. A half-dollar put in the palm of his hand he called a dollar. He said a wooden dumb-

bell, weighing half a pound, weighed about five pounds. The right foot, toes, and leg were somewhat more paralysed than the arm. The sensation was in nearly the same condition as in the arm."

Dyslexia, agraphia, intelligence good. He could only walk with help. Gradual intensification of symptoms with headache

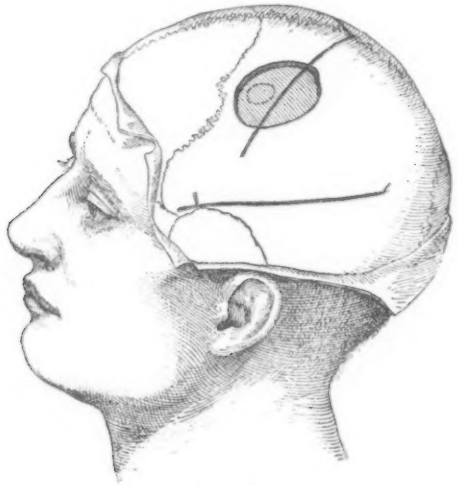


FIG. 10.

Case 15. Starr. The situation of the opening made in the skull.

until fourth day, when operation was done. Depressed circular fracture formed as indicated in inner circle (fig. 11).

A tarry, firm, extradural blood clot three-quarters of an inch thick at centre of circle found and removed. Gradual improvement—the muscular sense being last to recover. He was well three months after operation.—Hudson, *Annals of Surgery*, 1893, p. 421.

*Case* 17.—Male, 25. Blow on head, followed by right hemiplegia and complete motor aphasia, with twitchings of muscles of right hand and arm. He experienced some sensation in arm and leg, but apparently *none in the face*. Operation second day, removal of intradural clot, three ounces of blood removed; clot was three inches square and a quarter of an inch thick. Button of bone removed; it was over base of third left

frontal convolution. Complete recovery.—Mynter, *Annals of Surgery*, May, 1894, p. 539.

*Case* 18.—Male, aged 23. Compound fracture of the skull, and wound of the arm centre. History of blow on the right side of the head, with compound fracture; marked depression and extensive comminution—the depression being at the centre of the Rolandic region. The left arm below the elbow

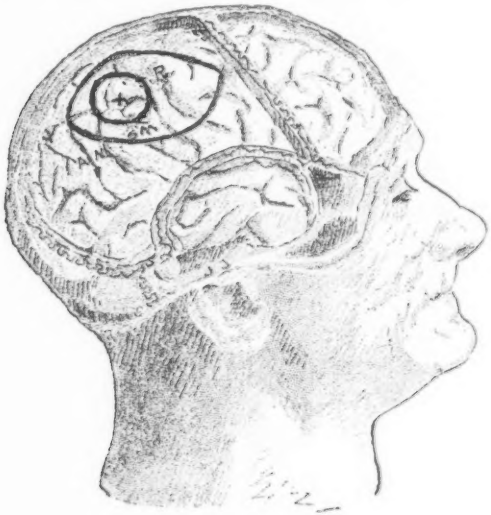


FIG. 11.

Case 16. Hudson. Showing location of clot.

was completely paralysed. The intellect was unimpaired, and sensation normal.

Operation three hours later. There was found a laceration of the surface of the brain three-fourths of an inch long, with slight loss of substance. After recovery patient had paræsthesia in left arm and leg. He developed hernia cerebri. Three months later the patient was found to have partial paralysis of the left arm and leg. Some time later the author states that examination showed still the presence of anæsthesia of the fingers and some rigidity of the forearm muscles.—Williams, *New York Med. Journ.*, January 9, 1892. "Motion at shoulder almost normal; can flex and extend the elbow and wrist; pronation and supination perfect; can flex fingers, but cannot com-

pletely extend them. All of the fingers of the left hand are partially anæsthetic, but not analgesic. Perception of heat and cold is normal; the tactile sense alone is affected. He picks up articles with difficulty—fumbles with them as a child would. With his eyes shut he cannot pick up a book, and cannot distinguish between a knife and a pencil held in his hand. The persistence of numbness in the fingers has been noted in a number of cases involving injury of the cortical motor area, and would appear to indicate, at least, a very close relation between the centres for motion and sensation. The inability to pick up articles with the eyes closed, and the awkwardness manifested in picking them up at all, seem to indicate faculty co-ordination, although these symptoms may be partly due to anæsthesia of the fingers."

*Case* 19.—The patient was a girl, aged 15, affected with Jacksonian epilepsy and progressive paralysis of left upper and lower limbs. Operation and removal of tumour the size of a hen's egg from the right central convolutions. Operation followed by paralysis, which greatly improved. Tactile, general, thermal, painful, and muscular sense impressions, which, before the operation, were intact, were affected in a certain measure after the operation over the whole left half of the body except the face.—Albertoni and Brigatti, *Rev. Sper. di Fren.*, xix., January 1, 1893.

*Case* 20.—Male, aged 18. History of a fall, followed by symptoms of development of cerebral abscess—headache, feverhebetude. Four weeks after fall Dr. Nason says: "I noticed left facial paralysis and paralysis of the left arm, with impairment of sensation (chiefly tactile sensation) over the paralysed areas. The tongue also deviated slightly to the left when protruded. I thought, too, that the left leg did not move quite so freely as the right. There was no paralysis of the ocular muscles, and the pupils were equal and reacted to light." Operation: Trephining "over lowest third of fissure of Rolando." An abscess was found opening on the lower third of the ascending frontal; about an ounce of pus was evacuated. On the third day after the operation he regained power in the leg; next day, power and sensation in shoulder and arm. Pain in left arm, face still paralysed. At the end of a week some power in left hand and partial return of sensation. Six weeks after operation "patient seems quite well, and but for fingers of hand being a little clumsy has completely recovered." "The mode of recovery from the paralysis goes to prove that the varicus cortical centres are centres for

associated movements and not for individual muscles; also, that sensation and motion are represented together in the central convolutions. It also would tend to prove that the centres for the various associated movements of the arm are placed from above downward in the following order: Shoulder, upper arm, forearm, wrist and hand, the thumb being lowest of all."

*Case* 21.—A woman, 55 years old. Glio-sarcoma of the corpus callosum. The patient had suffered for two years from some trouble in walking, but she could use her arms. She finally became dull and apathetic, and was admitted to the hospital. There was then a condition of mental dulness, slight facial paralysis on the left side, slight bilateral spastic paralysis with exaggerated reflexes. A very slight hemianæsthesia to pain obtained on the left side.

The *post-mortem* showed a very œdematous brain, with flattening of the convolutions. The two frontal lobes were united on their median surface. Upon the anterior portion of the corpus callosum there was a tumour which measured from one to three centimetres in diameter, and which grew on both sides into the brain substance, so that the total diameter of the tumour was from five to six centimetres. The centrum ovale was somewhat involved, and the observer thinks that the process might have affected the sensory part of the capsule. There was evidently an extensive destruction of the calloso-marginal gyrus on both sides, with practically no anæthesia.—Redtenbacher, *Ann. Rep. of the kk. Rudolf-Stiftung Hosp.*, 1891, p. 66.

*Case* 22.—Man, aged 46. Tumour of the brain, involving the central convolutions of the left hemisphere. The patient suffered from local epilepsy, involving the right arm, and finally with a paralysis and anæsthesia of the right arm and leg.

Operation and removal of the tumour the size of a hen's egg from the middle of the two left central convolutions. The tumour was a sarcoma. After removal of the tumour sensation returned, and also some motion.—Carson, *Jour. of Med.*, 1891, p. 31.

*Case* 23.—Male, aged 42. History: A blow on the head, followed by symptoms of the development of an abscess. Partial paralysis of left side, including face, arm and leg. Sensibility diminished in the left arm. Three days later, complete left hemiplegia, exaggerated reflexes, diminished cutaneous sensibility over arm, face and trunk.

Trephining over the fissure of Rolando. A trocar was plunged downward and forward to the depth of two inches, and six ounces of pus removed. Death followed. No record of autopsy.—Roy. *South. Med. Rec.*, 1890, p. 456.

*Case* 24.—Male, aged 21. History of intoxication followed by aphasia with symptoms of dulness of tactile sensation in the fingers, the palm and back of the hand, and wrist. The whole of

the right side, however, showed some defect in sensibility to touch, temperature, and pain, as well as of the muscle sense. Still it is stated that there was no ataxia in the right arm or hand. He could carry his right index to the tip of the nose, but he held the pen awkwardly and dropped it repeatedly. The symptoms increased, some paresis and some right hemiplegia developed, and the dulness of sensation increased proportionately.

Operation of trephining over the Rolandic fissure. A large subdural clot was found; this was removed, and the patient got well.

The sensory symptoms are specifically described as follows:

"Sensation (tested with a pin) is somewhat dulled on the whole of the right side. The main dulness is in the fingers,

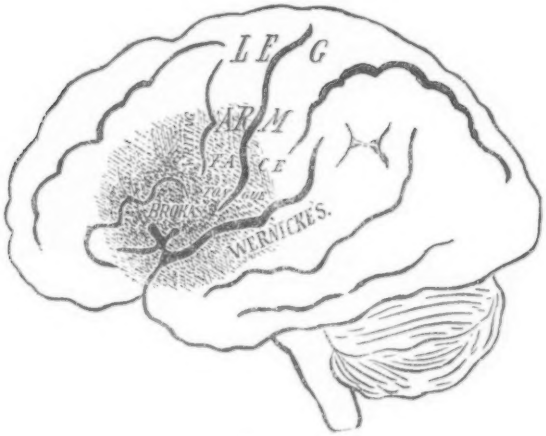



FIG. 12.

Case 21. Bremer and Carson. *American Journal of Medical Sciences*, February, 1892.

the palm and back of the hand, and the wrist; it is less higher up to the elbow and shoulder, and much less in the face. But, as just stated, the whole of the left side, including the leg, shows a defect in common sensibility. The same is true of the sense of temperature and pain. Passive movements of the fingers of the right side are not so well perceived as those of the left, showing a lowering of the muscle sense. The passive movements of the toes on the right side, however, are correctly stated. There is no ataxia in the right arm or hand; without hesitancy he carries his right index to the tip of the nose, the eyes being closed, and puts with precision the tip of the finger on the point of a pin.

On the fourth day after the operation: "Sensation in right arm still impaired. Sharp points on right arm recognised as

two points one and a-half inches apart, or fingers two inches apart. Unable to feel blowing of breath on hands or arm."

Discharged cured in three weeks.

The localisation of the lesion is given as shown in the accompanying diagram (fig. 12).

*Case* 25.—Male, aged 60. History of the gradual development of a brain tumour with progressive left hemiplegia, most marked in the left arm. Sensation diminished in both arm and leg; at times both arm and leg would be almost devoid of sensation, at other times hyperæsthesia was complained of. Gradual development of a complete hemiplegia with increasing hebetude, coma and death.

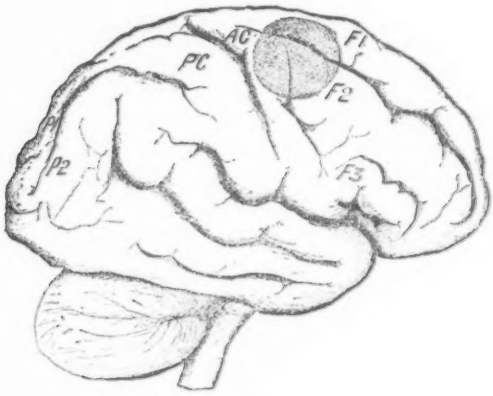



FIG. 31.

Case 25. Showing the localisation of the tumour which was adherent to the dura mater.

*Post-mortem.*—A tumour, two and a-half inches in diameter, was found involving the dura mater and the cortex of the middle of the precentral convolution and the posterior parts of the first and second frontal.—Barker, *N. Y. Med. Jour.*, June 25, 1892 (fig. 13).

Barker's words are: "Sensation diminished in both arm and leg. Dynamometer showed a loss of one-half in left hand." "The arm and leg became more paretic, sensation more disturbed. At times both arm and leg would be almost devoid of sensation (to pain and touch?); at other times hyperæsthesia was complained of."

An analysis of these cases shows first that injuries and destruction of the motor cortex are accompanied by disturbance of

cutaneous and musculo-articular sensations.[1] Before one can justly interpret the significance of these sensory disorders, we must agree upon some common interpretation of the significance of the tests used in making the examinations. The author's mode of procedure is shown in the following paragraph :—

(1) The tactile sense gives us sensations of touch, impact, pressure, and of modifications due to extent and character of the surface, so that we recognise smoothness, roughness, &c. It is tested by bringing some object carefully in contact with the skin, or by pressure on the surface, or by the drawing rough and smooth objects over the skin.

(2) The localisation of objects touching the skin is done by means of an associative process, by which former experiences in touch are revived. In localising an object the mental process is more complex than in simple appreciation of contact. While not strictly correct psychologically to say that tactile memories are revived, yet that term sufficiently expresses the idea. When a person loses his power of localising a point touched, and thinks it is on the thumb when it is on the middle finger, he has a tactile amnesia.

(3) The muscle-sense is dependent on the existence of sensory fibres in the muscles, joints and tendons. By it we appreciate the position of a limb, its active movements and its passive motions—*i.e.*, those made by another person. These sensations are tested in ways familiar to all, and their defects are shown in incoördination and inability to indicate, determine weights and the position or degree of motion of a limb.

(4) A more complex "sensation" is that known as active touch. It is the process by which one appreciates the nature of an object that is placed in the hand or on the skin. Thus the patient is made to distinguish between different coins, or between a key and a nail, &c. In this process both the tactile and muscular senses are brought into play, and here associative processes are called into play.

(5) Besides these we get thermal and painful sensations, the methods of testing which are familiar.

Now, in looking over the records of cases, it will be seen that the sensory losses most often observed are those in which the patient cannot localise an object, and in which he cannot tell the nature of an object ; that is to say, he loses the localisation power and the power of associating muscular and tactile sense, the power of active touch (Ziehen). Fumbling and awkwardness are clinical characteristics of destructive lesions of the motor cortex.

It is the associative power which is first and most impaired. After this we find most often tactile anæsthesia, then analgesia, then simple muscular anæsthesia, and least often loss of temperature sense.

[1] The author has not attempted to deal with the negative cases, in which cortical injury occurs without apparent sensory disturbance. The number of such cases is becoming yearly less.

This is in accordance with the evolutionary doctrine that the higher and more complex functions are more differentiated, more localised, and first affected by disease.

The simple tactile sensations are very diffusely represented in the cortex, and small lesions affect them slightly and temporarily, but the localising power, depending on tactile memories, and the "active touch," dependent on motor and tactile memories, are each associated with the special cortical motor centre for the particular part.

In small cortical lesions, therefore, we have (besides the paralysis) a kind of amnesia, which may be compared to the motor aphasia which results when Broca's centre is destroyed.

Naturally, before a set of motor nerve cells is discharged in a voluntary movement this discharge must be co-ordinated and set off in a definite manner. The skin-muscular sensations stored up as memories[1] regulate these voluntary and automatic movements just as the word memories regulate the organs of articulation. In cortical lesions there is then a skin and muscular "amnesia," and the patient with a cortical lesion is practically a case of motor-amnesia, so far as localisation and certain purposeful movements in the affected part are concerned. The application of the same psychology to the central convolutions that is applied to that of Broca solves, as it seems to me, the much-mooted question of the motor-cortex and its functions.

The other and concomitant symptoms of analgesia and thermo-anæsthesia can be equally understood on this hypothesis. Painful and thermic stimuli help in teaching the motor-cortex to discharge correctly and purposefully. Pain and thermic memories would naturally cluster around memories of contact and motion, yet they are less specialised, less important, less effective.

The muscular sensations have their cortical representation, probably in the inferior parietal lobule and its neighbourhood. But the awkward and fumbling movements in lesions of the central convolutions can be explained by the view suggested, that muscular memories or association processes are represented measurably, at least, in the motor area.

The author does not, however, subscribe to the doctrine of Bastian and others, who believe that the central convolutions are sensory centres. They are essentially motor. Nor is it enough to say that the motor-cortex is sensori-motor, for this does not imply the fact that the cortex represents not only sensations, but also memories of sensations. It is, in fact, a sensory-memory-motor organ.[2]

[1] As already stated, the term memory is used to make the description harmonise with our ordinary terminology in describing the effects of cortical lesions.

[2] The terms, "perception" or "association-revival" areas are perhaps more strictly correct from the psychologist's standpoint than memory areas. But the word, memory, as ordinarily used by neurologists, answers the present purpose.